



With the first and only IV mTOR inhibitor indicated for patients with advanced renal cell carcinoma (RCC)¹...

Change expectations for overall survival



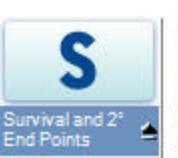
Please see Important Safety Information:

- Hypersensitivity reactions manifested by symptoms, including, but not limited to anaphylaxis, dyspnea, flushing, and chest pain have been observed with TORISEL.
 - Serum glucose, serum cholesterol, and triglycerides should be tested before and during treatment with TORISEL.

The use of TUDICEL is likely to result in hypoglycemia and hypotension. This may result in the need for



Cover



Survival and 2^o
End Points



ability and



1



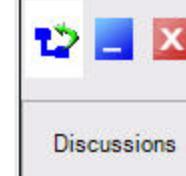
Reimburse



Study Design



Summary



Discussions

With the first and only IV mTOR inhibitor
indicated for patients with advanced
renal cell carcinoma (RCC)¹...

Change expectations for overall survival



Safety

Please see Important Safety Information:

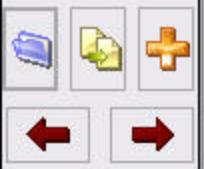
Hypersensitivity reactions manifested by symptoms, including, but not limited to anaphylaxis, dyspnea, flushing, and chest pain have been observed with TORISEL.

Serum glucose, serum cholesterol, and triglycerides should be tested before and during treatment with TORISEL.

The use of TORISEL is likely to result in hyperglycemia and hyperlipidemia. This may result in the need for



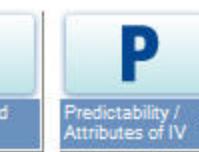
- CYP3A
- Hudes Reprint
- J Code Form
- Risk Factors



Cover



Survival and 2nd End Points



Tolerability and Safety



Predictability / Attributes of IV



NCCN Recommendation



Reimbursement Support



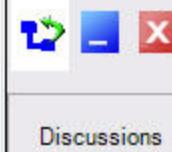
Study Design



Mechanism of Action



Summary



Discussions



With the first and only IV mTOR inhibitor
indicated for patients with advanced
renal cell carcinoma (RCC)¹...

References

1. TORISEL® Kit (temsirolimus) Prescribing Information, Wyeth Pharmaceuticals Inc.



Safety
Info

Please see
Prescribing
Information

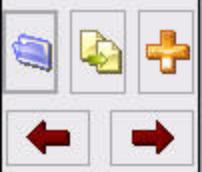
Please see Important Safety Information:

- Hypersensitivity reactions manifested by symptoms, including, but not limited to anaphylaxis, dyspnea, flushing, and chest pain have been observed with TORISEL.
- Serum glucose, serum cholesterol, and triglycerides should be tested before and during treatment with TORISEL.

The use of TORISEL is likely to result in hyperglycemia and hyperlipidemia. This may result in the need for



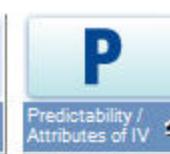
TORISEL[®]
(temsirolimus) injection



Cover



Survival and 2nd
End Points



Tolerability and
Safety



Predictability /
Attributes of IV



NCCN
Recommendation



Reimbursement
Support



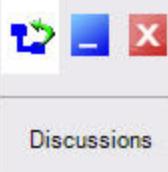
Study Design



Mechanism of
Action



Summary



Discussions

Please see Important Safety Information:

- Hypersensitivity reactions manifested by symptoms, including, but not limited to anaphylaxis, dyspnea, flushing, and chest pain have been observed with TORISEL.
- Serum glucose, serum cholesterol, and triglycerides should be tested before and during treatment with TORISEL.
 - The use of TORISEL is likely to result in hyperglycemia and hyperlipidemia. This may result in the need for an increase in the dose of, or initiation of, insulin and/or oral hypoglycemic agent therapy and/or lipid-lowering agents, respectively.
- The use of TORISEL may result in immunosuppression. Patients should be carefully observed for the occurrence of infections, including opportunistic infections.
- Cases of interstitial lung disease, some resulting in death, have occurred. Some patients were asymptomatic and others presented with symptoms. Some patients required discontinuation of TORISEL and/or treatment with corticosteroids and/or antibiotics.
- Cases of fatal bowel perforation occurred with TORISEL. These patients presented with fever, abdominal pain, metabolic acidosis, bloody stools, diarrhea, and/or acute abdomen.
- Cases of rapidly progressive and sometimes fatal acute renal failure not clearly related to disease progression occurred in patients who received TORISEL.
- Due to abnormal wound healing, use TORISEL with caution in the perioperative period.
- Patients with central nervous system tumors (primary CNS tumor or metastases) and/or receiving anticoagulation therapy may be at an increased risk of developing intracerebral bleeding (including fatal outcomes) while receiving TORISEL.
- Live vaccinations and close contact with those who received live vaccines should be avoided.
- Patients and their partners should be advised to avoid pregnancy throughout treatment and for 3 months after TORISEL therapy has stopped.
- The most common (incidence $\geq 30\%$) adverse reactions observed with TORISEL are: rash (47%), asthenia (51%), mucositis (41%), nausea (37%), edema (35%), and anorexia (32%). The most common laboratory abnormalities (incidence $\geq 30\%$) are anemia (94%), hyperglycemia (89%), hyperlipidemia (87%), hypertriglyceridemia (83%), elevated alkaline phosphatase (68%), elevated serum creatinine (57%), lymphopenia (53%), hypophosphatemia (49%), thrombocytopenia (40%), elevated AST (38%), and leukopenia (32%).
- Most common grades 3/4 adverse events and laboratory abnormalities included asthenia (11%), dyspnea (9%), hemoglobin decreased (20%), lymphocytes decreased (16%), glucose increased (16%), phosphorus decreased (18%), and triglycerides increased (44%).
- Strong inducers of CYP3A4/5 (eg, dexamethasone, rifampin) and strong inhibitors of CYP3A4 (eg, ketoconazole, atazanavir) may decrease and increase concentrations of the major metabolite of TORISEL, respectively. If alternatives cannot be used, dose modifications of TORISEL are recommended.

Scroll Up

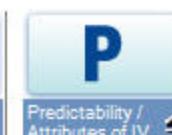
Scroll Down

Safety Info

Please see Prescribing Information

TOR inhibitor
with advanced
cancer (RCC)¹...

RISEL[®]
Sorafenib
Opimus) injection



Discussions

Please see Important Safety Information:

- Lowering agents, respectively.
- The use of TORISEL may result in immunosuppression. Patients should be carefully observed for the occurrence of infections, including opportunistic infections.
 - Cases of interstitial lung disease, some resulting in death, have occurred. Some patients were asymptomatic and others presented with symptoms. Some patients required discontinuation of TORISEL and/or treatment with corticosteroids and/or antibiotics.
 - Cases of fatal bowel perforation occurred with TORISEL. These patients presented with fever, abdominal pain, metabolic acidosis, bloody stools, diarrhea, and/or acute abdomen.
 - Cases of rapidly progressive and sometimes fatal acute renal failure not clearly related to disease progression occurred in patients who received TORISEL.
 - Due to abnormal wound healing, use TORISEL with caution in the perioperative period.
 - Patients with central nervous system tumors (primary CNS tumor or metastases) and/or receiving anticoagulation therapy may be at an increased risk of developing intracerebral bleeding (including fatal outcomes) while receiving TORISEL.
 - Live vaccinations and close contact with those who received live vaccines should be avoided.
 - Patients and their partners should be advised to avoid pregnancy throughout treatment and for 3 months after TORISEL therapy has stopped.
 - The most common (incidence $\geq 30\%$) adverse reactions observed with TORISEL are: rash (47%), asthenia (51%), mucositis (41%), nausea (37%), edema (35%), and anorexia (32%). The most common laboratory abnormalities (incidence $\geq 30\%$) are anemia (94%), hyperglycemia (89%), hyperlipidemia (87%), hypertriglyceridemia (83%), elevated alkaline phosphatase (68%), elevated serum creatinine (57%), lymphopenia (53%), hypophosphatemia (49%), thrombocytopenia (40%), elevated AST (38%), and leukopenia (32%).
 - Most common grades 3/4 adverse events and laboratory abnormalities included asthenia (11%), dyspnea (9%), hemoglobin decreased (20%), lymphocytes decreased (16%), glucose increased (16%), phosphorus decreased (18%), and triglycerides increased (44%).
 - Strong inducers of CYP3A4/5 (eg, dexamethasone, rifampin) and strong inhibitors of CYP3A4 (eg, ketoconazole, atazanavir) may decrease and increase concentrations of the major metabolite of TORISEL, respectively. If alternatives cannot be used, dose modifications of TORISEL are recommended.
 - St. John's Wort may decrease TORISEL plasma concentrations, and grapefruit juice may increase plasma concentrations of the major metabolite of TORISEL, and therefore both should be avoided.
 - The combination of TORISEL and sunitinib resulted in dose-limiting toxicity (Grade 3/4 erythematous maculopapular rash, and gout/cellulitis requiring hospitalization).

Scroll Up

Scroll Down

TOR inhibitor
with advanced
cancer (RCC)¹...



Safety
Info

Please see
Prescribing
Information

RISEL[®]
Sorafenib
Opimus) injection



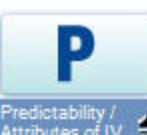
Cover



Survival and 2nd
End Points



Tolerability and
Safety



Predictability /
Attributes of IV



NCCN
Recommendation



Reimbursement
Support



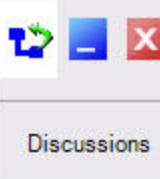
Study Design



Mechanism of
Action



Summary



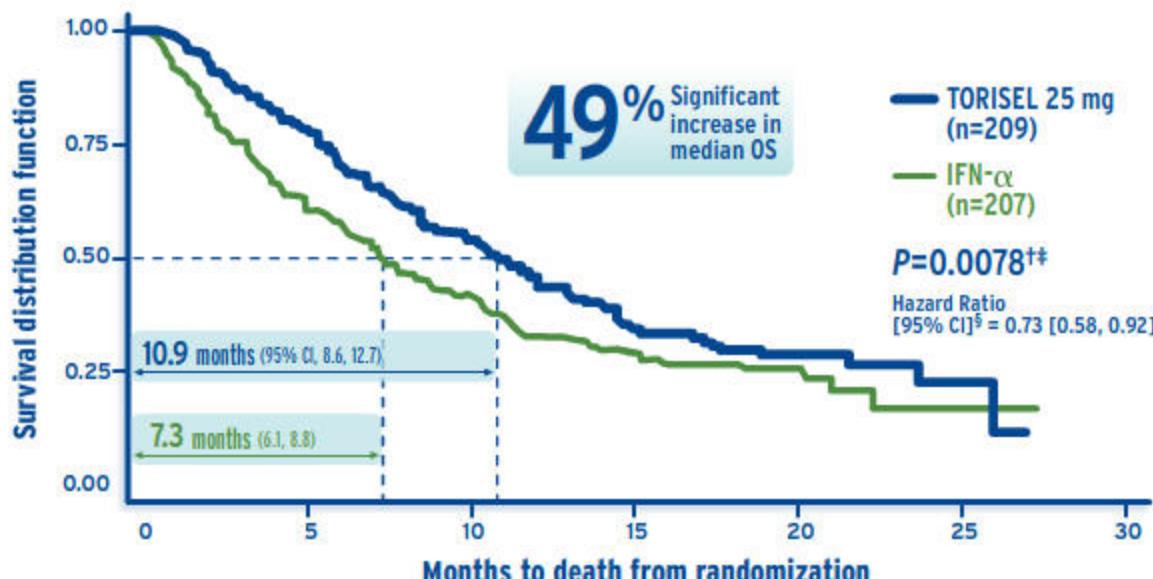
Discussions



TORISEL®—The first and only IV mTOR inhibitor indicated for advanced RCC¹

Overall survival benefit achieved as first-line therapy¹

Kaplan-Meier curves for overall survival (OS)*—TORISEL vs. IFN- α ¹



Results from a phase 3, multicenter, 3-arm, randomized, open-label study conducted in 626 previously untreated patients with advanced RCC.¹
See Study Design screen for more details on study design.

Please see Important Safety Information:

- Hypersensitivity reactions manifested by symptoms, including, but not limited to anaphylaxis, dyspnea, flushing, and chest pain have been observed with TORISEL.
- Serum glucose, serum cholesterol, and triglycerides should be tested before and during treatment with TORISEL.

The use of TORISEL is likely to result in hyperglycemia and hyperlipidemia. This may result in the need for

This was first-line treatment in patients with ≥ 3 of 6 preselected prognostic risk factors.¹

Overall survival benefit was achieved in patients with²

- Clear-cell or non-clear-cell tumor histology
- Any nephrectomy status

Median duration of treatment was 17 weeks (range 1-126 weeks) for TORISEL and 8 weeks (range 1-124 weeks) for IFN- α .¹

mTOR=mammalian target of rapamycin.

IFN- α =interferon-alpha.

CI=confidence interval.

* Time from randomization to death.

† A comparison is considered statistically significant if the P-value is <0.0159 (O'Brien-Fleming boundary at 446 deaths).

‡ Based on log-rank test stratified by prior nephrectomy and region.

§ Based on Cox proportional hazard model stratified by prior nephrectomy and region.



Safety
Info

Please see
Prescribing
Information



Cover



Survival and 2°
End Points



Tolerability and
Safety



Predictability /
Attributes of IV



NCCN
Recommendation



Reimbursement
Support



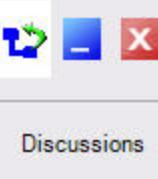
Study
Design



MOA



Summary



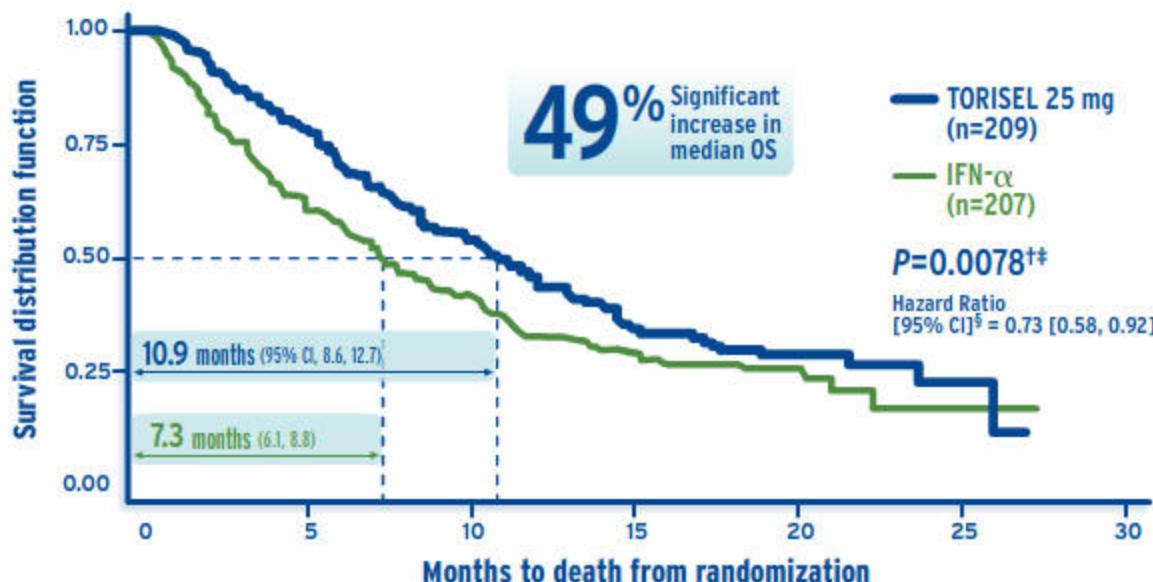
Discussions



TORISEL—The first and only IV mTOR inhibitor indicated for advanced RCC¹

Overall survival benefit achieved as first-line therapy¹

Kaplan-Meier curves for overall survival (OS)*—TORISEL vs. IFN- α ¹



Results from a phase 3, multicenter, 3-arm, randomized, open-label study conducted in 626 previously untreated patients with advanced RCC.¹
See Study Design screen for more details on study design.

This was first-line treatment in patients with ≥ 3 of 6 preselected prognostic risk factors.¹

Overall survival benefit was achieved in patients with²

- Clear-cell or non-clear-cell tumor histology
- Any nephrectomy status

Median duration of treatment was 17 weeks (range 1-126 weeks) for TORISEL and 8 weeks (range 1-124 weeks) for IFN- α .¹

mTOR=mammalian target of rapamycin.

IFN- α =interferon-alpha.

CI=confidence interval.

* Time from randomization to death.

† A comparison is considered statistically significant if the P-value is <0.0159 (O'Brien-Fleming boundary at 446 deaths).

‡ Based on log-rank test stratified by prior nephrectomy and region.

§ Based on Cox proportional hazard model stratified by prior nephrectomy and region.

Survival and
2° End Points

Overall Survival
(1° End Point)

Secondary
End Points

Please see Important Safety Information:

- Hypersensitivity reactions manifested by symptoms, including, but not limited to anaphylaxis, dyspnea, flushing, and chest pain have been observed with TORISEL.
- Serum glucose, serum cholesterol, and triglycerides should be tested before and during treatment with TORISEL.

The use of TORISEL is likely to result in hyperglycemia and hyperlipidemia. This may result in the need for

TORISEL®
(temsirolimus) injection
Change expectations



Safety
Info

Please see
Prescribing
Information

Change
expectations

Cover

S **T**
Hudes Reprint
End Points Safety

P Predictability / Attributes of IV
Safety

NCCN
NCCN Recommendation

Support
Reimbursement Support

Study Design
Study Design

MOA
Mechanism of Action

Summary
Summary

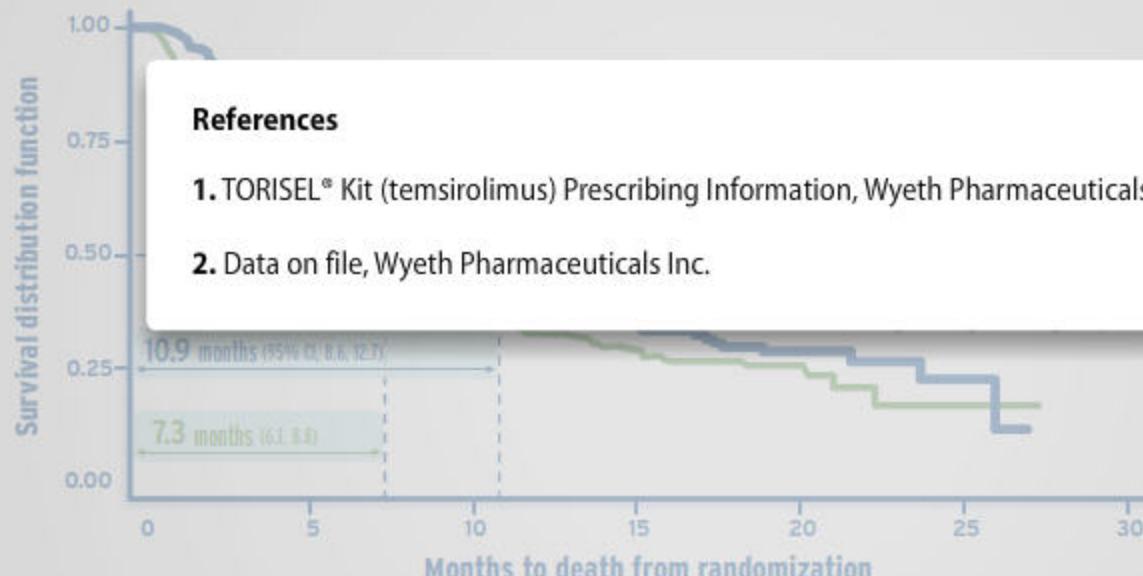
Discussions



TORISEL®—The first and only IV mTOR inhibitor indicated for advanced RCC¹

Overall survival benefit achieved as first-line therapy¹

Kaplan-Meier curves for overall survival (OS)*—TORISEL vs. IFN- α ¹



Results from a phase 3, multicenter, 3-arm, randomized, open-label study conducted in 626 previously untreated patients with advanced RCC.¹
See Study Design screen for more details on study design.

This was first-line treatment in patients with ≥ 3 of 6 preselected prognostic risk factors.¹

Overall survival benefit was seen in patients with²
• non-clear-cell tumor histology
• no prior nephrectomy status

Duration of treatment was 17 weeks (range 1-124 weeks) for TORISEL and 8 weeks (range 1-124 weeks) for IFN- α .¹

mTOR=mammalian target of rapamycin.
IFN- α =interferon-alpha.

CI=confidence interval.

* Time from randomization to death.

[†] A comparison is considered statistically significant if the P-value is <0.0159 (O'Brien-Fleming boundary at 446 deaths).

[‡] Based on log-rank test stratified by prior nephrectomy and region.

[§] Based on Cox proportional hazard model stratified by prior nephrectomy and region.

Please see Important Safety Information:

- Hypersensitivity reactions manifested by symptoms, including, but not limited to anaphylaxis, dyspnea, flushing, and chest pain have been observed with TORISEL.
- Serum glucose, serum cholesterol, and triglycerides should be tested before and during treatment with TORISEL.

The use of TORISEL is likely to result in hyperglycemia and hyperlipidemia. This may result in the need for

TORISEL
(temsirolimus) injection
Change expectations

Safety Info

Please see
**Prescribing
Information**



**Change
expectations**

Cover

S

Survival and 2[°]
End Points

T

Tolerability and
Safety

P

Predictability /
Attributes of IV

NCCN

NCCN
Recommendation

Support

Reimbursement
Support

**Study
Design**

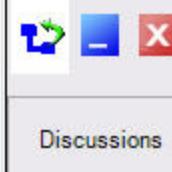
Study Design

MOA

Mechanism of
Action

Summary

Summary



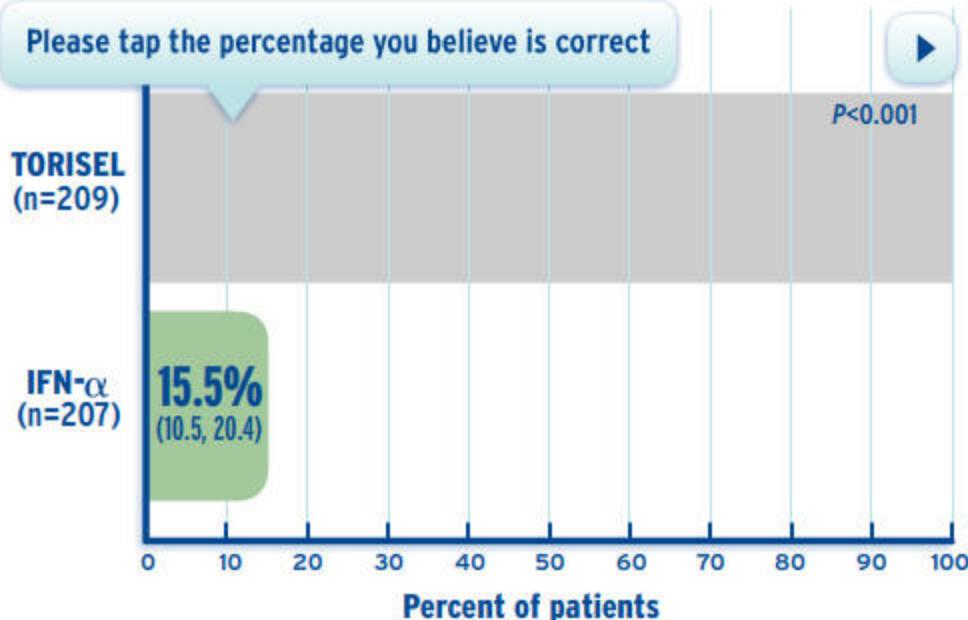
Discussions



Secondary End Points

TORISEL patients experienced a clinical benefit*
(CR/PR/SD ≥6 months)¹

Please tap the percentage you believe is correct



Progression-free survival (PFS)[†]

Patients receiving TORISEL experienced a significant 77% increase in median PFS compared with IFN- α ($P=0.0001^{§}$)²

- 5.5 months (95% CI, 3.9, 7.0) vs. 3.1 months (2.2, 3.8), respectively²

Overall response rate^{||}

8.6% (95% CI, 4.8, 12.4) of patients receiving TORISEL achieved an overall response compared with 4.8% (1.9, 7.8) of patients receiving IFN- α ($P=0.1232^{¶}$)²

Median duration of treatment was 17 weeks (range 1-126 weeks) for TORISEL and 8 weeks (range 1-124 weeks) for IFN- α .²

IFN- α =interferon-alpha. CI=confidence interval.

* Percent of patients who had confirmed complete response (CR), partial response (PR), or stable disease (SD) lasting at least 24 weeks as their best response to treatment. The evaluation of clinical benefit was based on blinded independent radiologic assessment of tumor response using RECIST-based criteria.

† Time from randomization to disease progression, censored at the last tumor evaluation date. The evaluation of progression-free survival (PFS) was based on blinded independent radiologic assessment of tumor response using RECIST-based criteria.

‡ Based on log-rank test stratified by prior nephrectomy and region.

§ Not adjusted for multiple comparisons.

|| Percent of patients who had confirmed CR or PR as their best response to treatment. The evaluation of overall response rate as based on blinded independent radiologic assessment of tumor response using RECIST-based criteria.

¹ Based on Cochran-Mantel-Haenszel test stratified by prior nephrectomy and region.

Please see Important Safety Information:

- Hypersensitivity reactions manifested by symptoms, including, but not limited to anaphylaxis, dyspnea, flushing, and chest pain have been observed with TORISEL.
- Serum glucose, serum cholesterol, and triglycerides should be tested before and during treatment with TORISEL.

The use of TORISEL is likely to result in hyperglycemia and hyperlipidemia. This may result in the need for

TORISEL®
 (temsirolimus) injection
 Change expectations



Safety
Info

Please see
Prescribing
Information



Cover



Survival and 2°
End Points



Tolerability and
Safety



Predictability /
Attributes of IV



NCCN
Recommendation



Reimbursement
Support



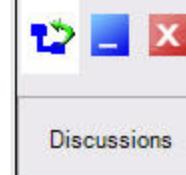
Study Design



Mechanism of
Action



Summary



Discussions



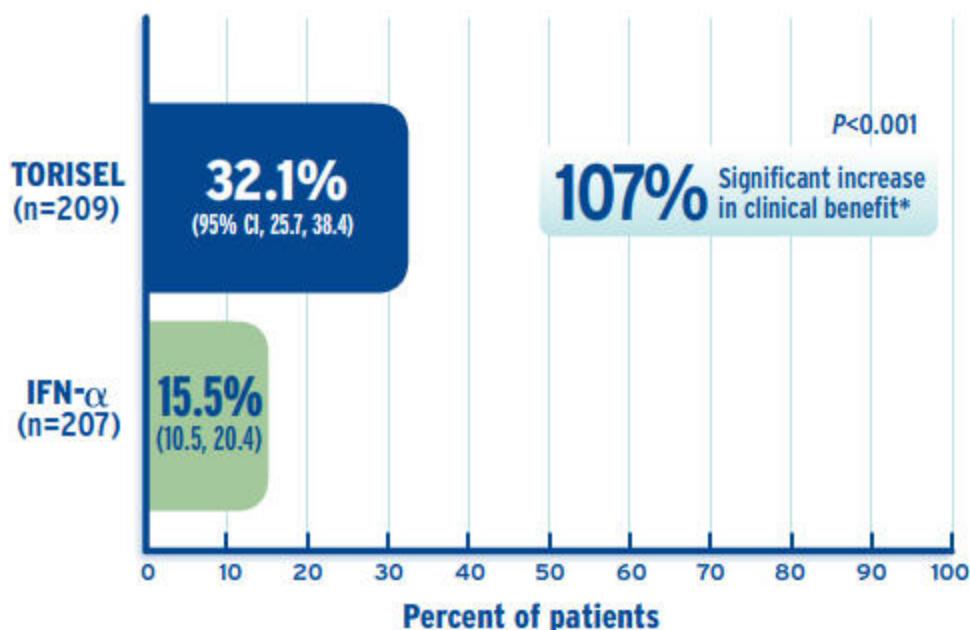
Secondary End Points

Twice as many TORISEL patients experienced a clinical benefit*
(CR/PR/SD ≥6 months)¹

Survival and
2° End Points

Overall Survival
(1° End Point)

Secondary
End Points



Progression-free survival (PFS)[†]

Patients receiving TORISEL experienced a significant 77% increase in median PFS compared with IFN- α ($P=0.0001^{\ddagger\$}$)²

- 5.5 months (95% CI, 3.9, 7.0) vs. 3.1 months (2.2, 3.8), respectively²

Overall response rate^{||}

8.6% (95% CI, 4.8, 12.4) of patients receiving TORISEL achieved an overall response compared with 4.8% (1.9, 7.8) of patients receiving IFN- α ($P=0.1232^{\ddagger\$}$)²

Median duration of treatment was 17 weeks (range 1-126 weeks) for TORISEL and 8 weeks (range 1-124 weeks) for IFN- α .²

IFN- α =interferon-alpha. CI=confidence interval.

* Percent of patients who had confirmed complete response (CR), partial response (PR), or stable disease (SD) lasting at least 24 weeks as their best response to treatment. The evaluation of clinical benefit was based on blinded independent radiologic assessment of tumor response using RECIST-based criteria.

[†] Time from randomization to disease progression, censored at the last tumor evaluation date. The evaluation of progression-free survival (PFS) was based on blinded independent radiologic assessment of tumor response using RECIST-based criteria.

[‡] Based on log-rank test stratified by prior nephrectomy and region.

[§] Not adjusted for multiple comparisons.

^{||} Percent of patients who had confirmed CR or PR as their best response to treatment. The evaluation of overall response rate as based on blinded independent radiologic assessment of tumor response using RECIST-based criteria.

[¶] Based on Cochran-Mantel-Haenszel test stratified by prior nephrectomy and region.

Safety Info



Please see
Prescribing
Information



Please see Important Safety Information:

- Hypersensitivity reactions manifested by symptoms, including, but not limited to anaphylaxis, dyspnea, flushing, and chest pain have been observed with TORISEL.
- Serum glucose, serum cholesterol, and triglycerides should be tested before and during treatment with TORISEL.

The use of TORISEL is likely to result in hyperglycemia and hyperlipidemia. This may result in the need for

TORISEL
(temsirolimus) injection
Change expectations

Change
expectations

Cover

S
Survival and 2°
End Points

Survival and 2°
End Points

T
Tolerability and
Safety

Tolerability and
Safety

P
Predictability /
Attributes of IV

Predictability /
Attributes of IV

NCCN
NCCN
Recommendation

NCCN
Recommendation

Support
Reimbursement
Support

Reimbursement
Support

Study Design
Study Design

Study Design

MOA
Mechanism of
Action

Mechanism of
Action

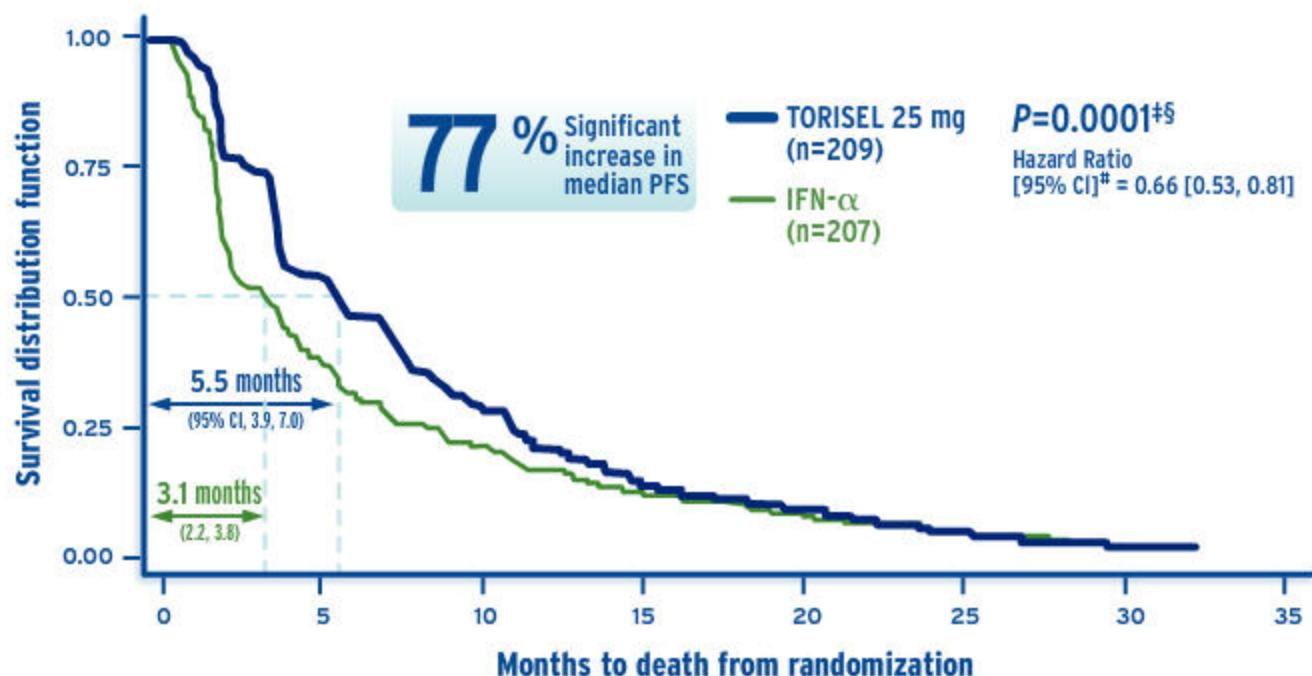
Summary
Summary

Summary

Discussions

Discussions

Kaplan-Meier Curves for PFS[†]-TORISEL vs. IFN- α



[†] Time from randomization to disease progression, censored at the last tumor evaluation date. The evaluation of PFS was based on blinded independent radiologic assessment of tumor response using RECIST-based criteria.

[#] Based on log-rank test, stratified by prior nephrectomy and region.

[§] Not adjusted for multiple comparisons.

[‡] Based on Cox proportional hazard model stratified by prior nephrectomy and region.

[†] Based on Cochran-Mantel-Haenszel test stratified by prior nephrectomy and region.

Please see Important Safety Information:

- Hypersensitivity reactions manifested by symptoms, including, but not limited to anaphylaxis, dyspnea, flushing, and chest pain have been observed with TORISEL.
- Serum glucose, serum cholesterol, and triglycerides should be tested before and during treatment with TORISEL.

The use of TORISEL is likely to result in hyperglycemia and hyperlipidemia. This may result in the need for

TORISEL
(temsirolimus) injection
Change expectations

Safety Info



Please see Prescribing Information



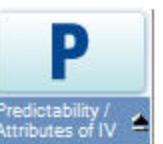
Cover



Survival and 2° End Points



Tolerability and Safety



Predictability / Attributes of IV



NCCN Recommendation



Reimbursement Support



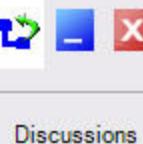
Study Design



Mechanism of Action



Summary



Discussions

Median overall response rates^{||} in the phase 3 clinical trial

Secondary
End Points

Twice as many
(CR/PR/SD)

Survival and
2° End Points

Overall Survival
(1° End Point)

Secondary
End Points

TORISEL
(n=209)

IFN- α
(n=207)

TORISEL
(n=209)

IFN- α
(n=207)

8.6%
(95% CI, 4.8, 12.4)

4.8%
(1.9, 7.8)

P=0.1232^{‡§¶}

79 % Increase in
median overall
response rate

Percent of patients

[‡] Based on log-rank test, stratified by prior nephrectomy and region.

[§] Not adjusted for multiple comparisons.

^{||} Percent of patients who had confirmed CR or PR as their best response to treatment. The evaluation of overall response rate was based on blinded independent radiologic assessment of tumor response using RECIST-based criteria.

[¶] Based on Cochran-Mantel-Haenszel test stratified by prior nephrectomy and region.

ival (PFS)[†]

xperienced a significant 77% increase compared with IFN- α (P=0.0001^{†‡}) (2.0 vs. 3.1 months (2.2, 3.8),

patients receiving TORISEL achieved a median overall survival of 17 weeks (range 1-126 weeks) compared with 12 weeks (range 1-124 weeks) for IFN- α .²

ce interval.
ned complete response (CR), partial response (PR) lasting at least 24 weeks as their best response. The evaluation of clinical benefit was based on blinded independent radiologic assessment of tumor response using RECIST-based criteria. The progression-free survival (PFS) was based on the assessment of tumor response using RECIST-based criteria.

prior nephrectomy and region.

ans.
ned CR or PR as their best response to treatment. The evaluation of overall response rate was based on blinded independent radiologic assessment of tumor response using RECIST-based criteria.

[†] Based on Cochran-Mantel-Haenszel test stratified by prior nephrectomy and region.

Please see Important Safety Information:

- Hypersensitivity reactions manifested by symptoms, including, but not limited to anaphylaxis, dyspnea, flushing, and chest pain have been observed with TORISEL.
- Serum glucose, serum cholesterol, and triglycerides should be tested before and during treatment with TORISEL.

The use of TORISEL is likely to result in hyperglycemia and hyperlipidemia. This may result in the need for

TORISEL®
(temsirolimus) injection
Change expectations



Please see
Prescribing
Information



Cover



Survival and 2°
End Points



Tolerability and
Safety



Predictability /
Attributes of IV



NCCN
Recommendation



Reimbursement
Support



Study Design



Mechanism of
Action



Summary



Discussions



Secondary End Points

Twice as many TORISEL patients experienced a clinical benefit*
(CR/PR/SD ≥6 months)¹

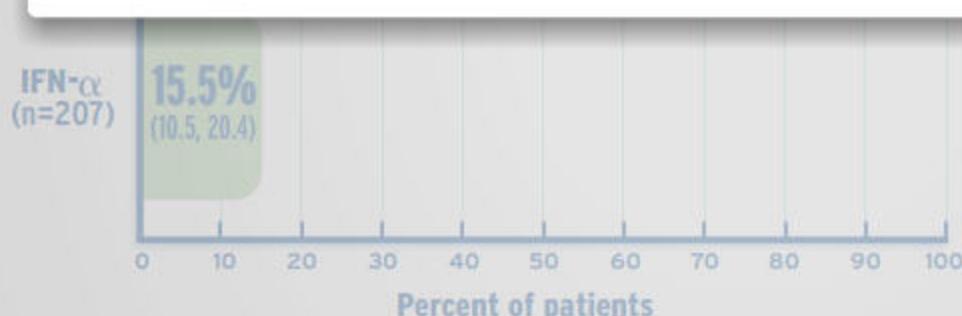
Survival and
2° End Points

Overall Survival
(1° End Point)

Secondary
End Points

References

- Hudes G, Carducci M, Tomczak P, et al. Temsirolimus, interferon alfa, or both for advanced renal-cell carcinoma. *N Engl J Med.* 2007;356:2271-2281.
- TORISEL® Kit (temsirolimus) Prescribing Information, Wyeth Pharmaceuticals Inc.



Progression-free survival (PFS)[†]

Patients receiving TORISEL experienced a significant 77% increase in median PFS compared with IFN- α ($P=0.0001^{‡}$)²

* 5.5 months (95% CI, 3.9, 7.0) vs. 3.1 months (2.2, 3.8),²

living TORISEL achieved
(1.9, 7.8) of patients

weeks (range 1-126 weeks)
weeks) for IFN- α .²

IFN- α =interferon-alpha. CI=confidence interval.

* Percent of patients who had confirmed complete response (CR), partial response (PR), or stable disease (SD) lasting at least 24 weeks as their best response to treatment. The evaluation of clinical benefit was based on blinded independent radiologic assessment of tumor response using RECIST-based criteria.

[†] Time from randomization to disease progression, censored at the last tumor evaluation date. The evaluation of progression-free survival (PFS) was based on blinded independent radiologic assessment of tumor response using RECIST-based criteria.

[‡] Based on log-rank test stratified by prior nephrectomy and region.

[§] Not adjusted for multiple comparisons.

^{||} Percent of patients who had confirmed CR or PR as their best response to treatment. The evaluation of overall response rate as based on blinded independent radiologic assessment of tumor response using RECIST-based criteria.

[¶] Based on Cochran-Mantel-Haenszel test stratified by prior nephrectomy and region.

Safety
Info

Please see
Prescribing
Information

Please see Important Safety Information:

- Hypersensitivity reactions manifested by symptoms, including, but not limited to anaphylaxis, dyspnea, flushing, and chest pain have been observed with TORISEL.
- Serum glucose, serum cholesterol, and triglycerides should be tested before and during treatment with TORISEL.

The use of TORISEL is likely to result in hyperglycemia and hyperlipidemia. This may result in the need for

TORISEL
(temsirolimus) injection
Change expectations

Change
expectations

Cover

S

Survival and 2°
End Points

T

Tolerability and
Safety

P

Predictability /
Attributes of IV

NCCN

NCCN
Recommendation

Support

Reimbursement
Support

Study Design

Study Design

MOA

Mechanism of
Action

Summary

Summary

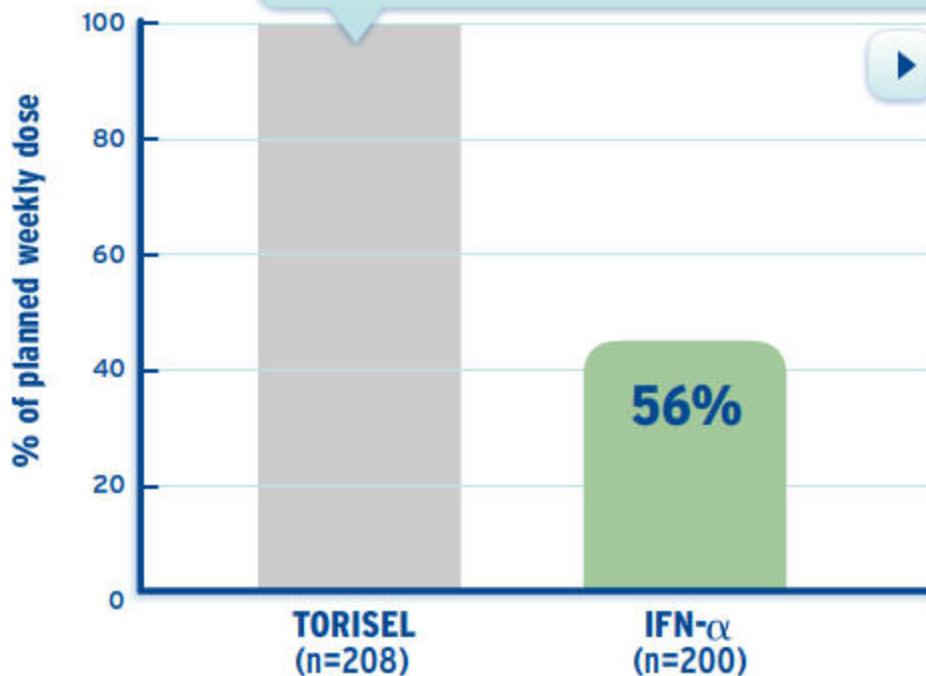
Discussions



Tolerability—Planned Weekly Dose

TORISEL patients on average received _____ of the planned weekly IV dose¹

Please tap the percentage you believe is correct



- TORISEL mean weekly dose was 23 mg, and the max planned weekly dose was 25 mg¹
- IFN- α mean weekly dose was 30 MU, and the max planned weekly dose was 54 MU¹

Please see Important Safety Information:

- Hypersensitivity reactions manifested by symptoms, including, but not limited to anaphylaxis, dyspnea, flushing, and chest pain have been observed with TORISEL.
- Serum glucose, serum cholesterol, and triglycerides should be tested before and during treatment with TORISEL.

The use of TORISEL is likely to result in hyperglycemia and hyperlipidemia. This may result in the need for

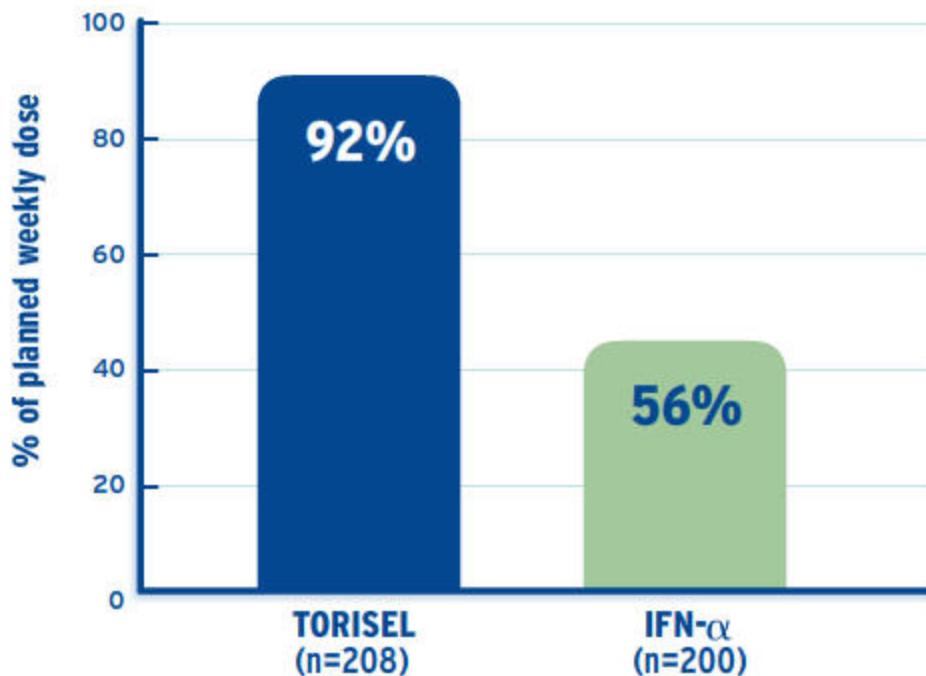
 **TORISEL**
(temsirolimus) injection
Change expectations



Tolerability–Planned Weekly Dose

TORISEL patients on average received 92% of the planned weekly IV dose¹

- Tolerability and Safety**
- Planned Weekly Dose
- Discontinuation Rates
- Grade 3 or 4 AEs $\geq 10\%$
- AEs $\geq 30\%$
- Cardiovascular Information
- Laboratory Abnormalities
- Hypersensitivity Information
- Adverse Reactions



- TORISEL mean weekly dose was 23 mg, and the max planned weekly dose was 25 mg¹
- IFN- α mean weekly dose was 30 MU, and the max planned weekly dose was 54 MU¹

Please see Important Safety Information:

- Hypersensitivity reactions manifested by symptoms, including, but not limited to anaphylaxis, dyspnea, flushing, and chest pain have been observed with TORISEL.
- Serum glucose, serum cholesterol, and triglycerides should be tested before and during treatment with TORISEL.

The use of TORISEL is likely to result in hyperglycemia and hyperlipidemia. This may result in the need for



- Safety Info**
- Please see Prescribing Information



Tolerability—Planned Weekly Dose

TORISEL patients on average received 92% of the planned weekly IV dose¹

Tolerability
and Safety

Planned
Weekly Dose

Discontinuation
Rates

Grade 3 or 4
AEs ≥10%

AEs ≥30%

Cardiovascular
Information

Laboratory
Abnormalities

Hypersensitivity
Information

Adverse
Reactions

Safety
Info

Please see
Prescribing
Information

References

1. Hudes G, Carducci M, Tomczak P, et al. Temsirolimus, interferon alfa, or both for advanced renal-cell carcinoma. *N Engl J Med.* 2007;356:2271-2281.



- TORISEL mean weekly dose was 23 mg, and the max planned weekly dose was 25 mg¹
- IFN- α mean weekly dose was 30 MU, and the max planned weekly dose was 54 MU¹

Please see Important Safety Information:

- Hypersensitivity reactions manifested by symptoms, including, but not limited to anaphylaxis, dyspnea, flushing, and chest pain have been observed with TORISEL.
- Serum glucose, serum cholesterol, and triglycerides should be tested before and during treatment with TORISEL.

The use of TORISEL is likely to result in hyperglycemia and hypertension. This may result in the need for antihypertensive and hypoglycemic agents.

TORISEL
(temsirolimus) injection
Change expectations



Change
expectations

Cover

S

Survival and 2nd
End Points

T

Tolerability and
Safety

P

Predictability /
Attributes of IV

NCCN

NCCN
Recommendation

Support

Reimbursement
Support

Study Design

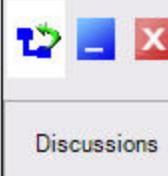
Study Design

MOA

Mechanism of
Action

Summary

Summary



Discussions



Tolerability–Discontinuation Rates

7.2% of patients discontinued TORISEL due to adverse events¹

Reason for Discontinuation	TORISEL (n=208)	IFN- α (n=200)
Adverse event	7.2%	14.5%
Symptomatic deterioration*	6.7%	14.0%
Patient request	3.8%	3.0%
Death	2.9%	5.0%
Other	1.0% [†]	2.0% [‡]
Protocol violation	0.5%	1.0%
Disease progression	73.6%	57.5%

* Patients with a global deterioration of health status requiring discontinuation of treatment without objective evidence of disease progression at that time should be classified as having "symptomatic deterioration."¹

[†] Other reasons for discontinuation in the TORISEL arm were disease progression and investigator's decision.¹

[‡] Other reasons for discontinuation in the IFN- α arm were lost to follow up, investigator's discretion, patient underwent surgery, and patient's request.¹



Safety Info

Please see Prescribing Information

Please see Important Safety Information:

- Hypersensitivity reactions manifested by symptoms, including, but not limited to anaphylaxis, dyspnea, flushing, and chest pain have been observed with TORISEL.
- Serum glucose, serum cholesterol, and triglycerides should be tested before and during treatment with TORISEL.

The use of TORISEL is likely to result in hyperglycemia and hyperlipidemia. This may result in the need for

TORISEL
(temsirolimus) injection
Change expectations





Tolerability–Discontinuation Rates

7.2% of patients discontinued TORISEL due to adverse events¹

Reason for Discontinuation	TORISEL (n=208)	IFN- α (n=200)
Adverse event*	7.2%	1.5%
Symptom†		
Patient request		
Death		
Other	1.0%‡	2.0%‡
Protocol violation	0.5%	1.0%
Disease progression	73.6%	57.5%

References

1. Data on file, Wyeth Pharmaceuticals Inc.

* Patients with a global deterioration of health status requiring discontinuation of treatment without objective evidence of disease progression at that time should be classified as having "symptomatic deterioration."¹

† Other reasons for discontinuation in the TORISEL arm were disease progression and investigator's decision.¹

‡ Other reasons for discontinuation in the IFN- α arm were lost to follow up, investigator's discretion, patient underwent surgery, and patient's request.¹

Please see Important Safety Information:

- Hypersensitivity reactions manifested by symptoms, including, but not limited to anaphylaxis, dyspnea, flushing, and chest pain have been observed with TORISEL.
- Serum glucose, serum cholesterol, and triglycerides should be tested before and during treatment with TORISEL.

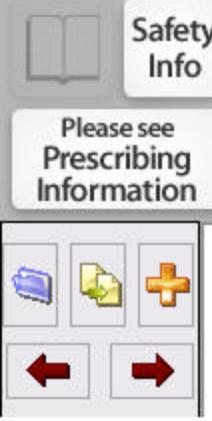
The use of TORISEL is likely to result in hyperglycemia and hyperlipidemia. This may result in the need for

 **TORISEL**
(temsirolimus) injection
Change expectations

- Tolerability and Safety
- Planned Weekly Dose
- Discontinuation Rates
- Grade 3 or 4 AEs $\geq 10\%$
- AEs $\geq 30\%$
- Cardiovascular Information
- Laboratory Abnormalities
- Hypersensitivity Information
- Adverse Reactions

Safety Info

Please see Prescribing Information



Cover



Survival and 2° End Points



Tolerability and Safety



Predictability / Attributes of IV



NCCN Recommendation



Reimbursement Support



Study Design



Mechanism of Action



Summary



Discussions



Tolerability—Grade 3 or 4 AEs $\geq 10\%$

Grade 3 or 4* laboratory abnormalities and adverse reaction at an incidence $\geq 10\%^1$

Grade 3 or 4 Laboratory Abnormality	Percent of Patients (n=208)
Hypertriglyceridemia	44%
Anemia	20%
Hypophosphatemia	18%
Lymphopenia [†]	16%
Hyperglycemia	16%
Grade 3 or 4 Adverse Reaction	
Asthenia	11%

* Common Toxicity Criteria (CTC) Version 3.0.

[†] Grade 1 toxicity may be under-reported for lymphocytes.

Please see Important Safety Information:

- Hypersensitivity reactions manifested by symptoms, including, but not limited to anaphylaxis, dyspnea, flushing, and chest pain have been observed with TORISEL.
- Serum glucose, serum cholesterol, and triglycerides should be tested before and during treatment with TORISEL.

The use of TORISEL is likely to result in hyperglycemia and hyperlipidemia. This may result in the need for

 **TORISEL**
(temsirolimus) injection
Change expectations



Safety
Info

Please see
Prescribing
Information



Cover



Survival and 2°
End Points



Tolerability and
Safety



Predictability /
Attributes of IV



NCCN
Recommendation



Reimbursement
Support



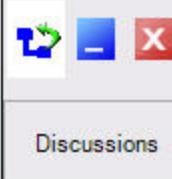
Study Design



Mechanism of
Action



Summary



Discussions



Tolerability—Grade 3 or 4 AEs $\geq 10\%$

Grade 3 or 4* laboratory abnormalities and adverse reaction at an incidence $\geq 10\%^1$

Tolerability and Safety
Planned Weekly Dose
Discontinuation Rates
Grade 3 or 4 AEs $\geq 10\%$
AEs $\geq 30\%$
Cardiovascular Information
Laboratory Abnormalities
Hypersensitivity Information
Adverse Reactions

Grade 3 or 4 Laboratory Abnormality	Percent of Patients (n=208)
Hypertension	16%
Anemia	16%
Hypophosphatemia	11%
Lymphopenia [†]	16%
Hyperglycemia	16%
Grade 3 or 4 Adverse Reaction	
Asthenia	11%

References

1. TORISEL® Kit (temsirolimus) Prescribing Information, Wyeth Pharmaceuticals Inc.

* Common Toxicity Criteria (CTC) Version 3.0.

[†] Grade 1 toxicity may be under-reported for lymphocytes.

Please see Important Safety Information:

- Hypersensitivity reactions manifested by symptoms, including, but not limited to anaphylaxis, dyspnea, flushing, and chest pain have been observed with TORISEL.
- Serum glucose, serum cholesterol, and triglycerides should be tested before and during treatment with TORISEL.

The use of TORISEL is likely to result in hyperglycemia and hyperlipidemia. This may result in the need for

 **TORISEL**
(temsirolimus) injection
Change expectations

Safety Info
Please see Prescribing Information

Change expectations	S	T	P	NCCN	Support	Study Design	MOA	Summary	Discussions
Cover	Survival and 2 nd End Points	Tolerability and Safety	Predictability / Attributes of IV	NCCN Recommendation	Reimbursement Support	Study Design	Mechanism of Action	Summary	Discussions



Tolerability-AEs $\geq 30\%$

Adverse reactions of all grades at an incidence $\geq 30\%^1$

Adverse Reaction	Percent of Patients (n=208)	
	All Grades	Grades 3&4
Asthenia	51%	11%
Rash* 	47%	5%
Mucositis†	41%	3%
Nausea	37%	2%
Edema‡	35%	3%
Anorexia	32%	3%

* Includes eczema, exfoliative dermatitis, maculopapular rash, pruritic rash, pustular rash, rash not otherwise specified (NOS), and vesiculobullous rash.

† Includes aphthous stomatitis, glossitis, mouth ulceration, mucositis, and stomatitis.

‡ Includes edema, facial edema, and peripheral edema.

Please see Important Safety Information:

- Hypersensitivity reactions manifested by symptoms, including, but not limited to anaphylaxis, dyspnea, flushing, and chest pain have been observed with TORISEL.
- Serum glucose, serum cholesterol, and triglycerides should be tested before and during treatment with TORISEL.

The use of TORISEL is likely to result in hyperglycemia and hyperlipidemia. This may result in the need for

 **TORISEL**
(temsirolimus) injection
Change expectations



Safety
Info

Please see
Prescribing
Information



Cover



Survival and 2°
End Points



Tolerability and
Safety



Predictability /
Attributes of IV



NCCN
Recommendation



Reimbursement
Support



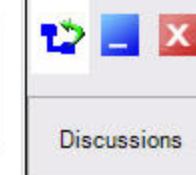
Study Design



Mechanism of
Action



Summary



Discussions



Tolerability
and Safety

Planned
Weekly Dose

Discontinuation
Rates

Grade 3 or 4
AEs ≥10%

AEs ≥30%

Cardiovascular
Information

Laboratory
Abnormalities

Hypersensitivity
Information

Adverse
Reactions



Safety
Info

Please see
Prescribing
Information



Pruritic Rash



Pruritic Maculopapular Rash

Courtesy of the Cleveland Clinic Taussig Cancer Institute

* Includes eczema, exfoliative dermatitis, maculopapular rash, pruritic rash, pustular rash, rash not otherwise specified (NOS), and vesiculobullous rash.

† Includes aphthous stomatitis, glossitis, mouth ulceration, mucositis, and stomatitis.

‡ Includes edema, facial edema, and peripheral edema.

Please see Important Safety Information:

- Hypersensitivity reactions manifested by symptoms, including, but not limited to anaphylaxis, dyspnea, flushing, and chest pain have been observed with TORISEL.
- Serum glucose, serum cholesterol, and triglycerides should be tested before and during treatment with TORISEL.

The use of TORISEL is likely to result in hyperglycemia and hyperlipidemia. This may result in the need for

TORISEL®
(temsirolimus) injection
Change expectations



Cover



Survival and 2°
End Points



Tolerability and
Safety



Predictability /
Attributes of IV



NCCN
Recommendation



Reimbursement
Support



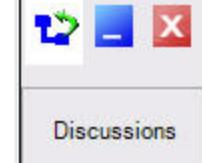
Study Design



Mechanism of
Action



Summary



Discussions



Tolerability-AEs $\geq 30\%$

Adverse reactions of all grades at an incidence $\geq 30\%^1$

Adverse Reaction	Percent of Patients (n=208)	
	All Grades	Grades 3&4
Asthenia	41%	3%
Rash*	37%	2%
Mucositis	37%	3%
Nausea	37%	2%
Edema†	35%	3%
Anorexia	32%	3%

References

1. TORISEL® Kit (temsirolimus) Prescribing Information, Wyeth Pharmaceuticals Inc.

* Includes eczema, exfoliative dermatitis, maculopapular rash, pruritic rash, pustular rash, rash not otherwise specified (NOS), and vesiculobullous rash.

† Includes aphthous stomatitis, glossitis, mouth ulceration, mucositis, and stomatitis.

‡ Includes edema, facial edema, and peripheral edema.

Please see Important Safety Information:

- Hypersensitivity reactions manifested by symptoms, including, but not limited to anaphylaxis, dyspnea, flushing, and chest pain have been observed with TORISEL.
- Serum glucose, serum cholesterol, and triglycerides should be tested before and during treatment with TORISEL.

The use of TORISEL is likely to result in hyperglycemia and hyperlipidemia. This may result in the need for

 **TORISEL**
(temsirolimus) injection
Change expectations

 Safety Info

Please see
Prescribing
Information



 Change
expectations

Cover

 S

Survival and 2nd
End Points

 T

Tolerability and
Safety

 P

Predictability /
Attributes of IV

 NCCN

NCCN
Recommendation

 Support

Reimbursement
Support

 Study Design

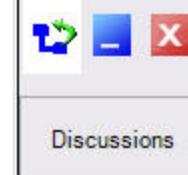
Study Design

 MOA

Mechanism of
Action

 Summary

Summary

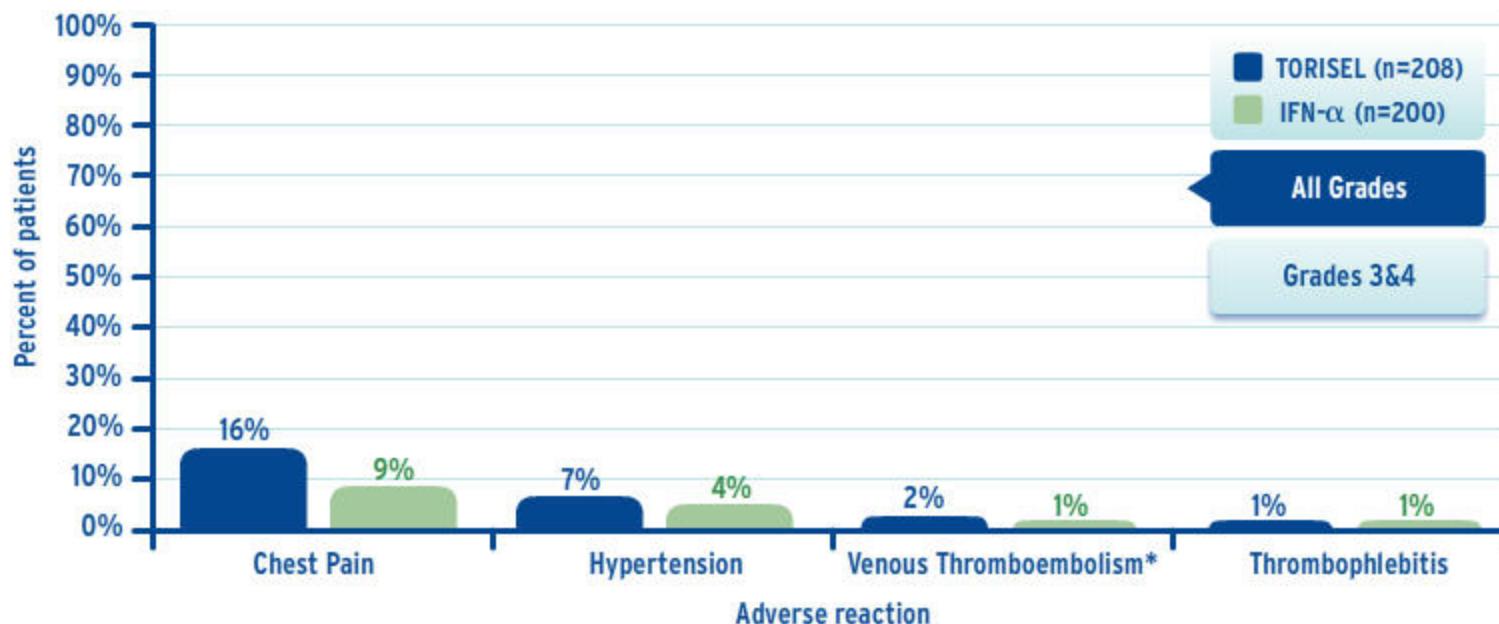


Discussions



Tolerability—Cardiovascular-related adverse reactions

Selected cardiovascular-related adverse reactions in the phase 3 trial of any grade^{1,2}



Intracerebral hemorrhage

- Patients with central nervous system tumors (primary CNS tumor or metastases) and/or receiving anticoagulation therapy may be at an increased risk of developing intracerebral bleeding (including fatal outcomes) while receiving TORISEL.

*Includes deep vein thrombosis and pulmonary embolus.

Please see Important Safety Information:

- Hypersensitivity reactions manifested by symptoms, including, but not limited to anaphylaxis, dyspnea, flushing, and chest pain have been observed with TORISEL.
- Serum glucose, serum cholesterol, and triglycerides should be tested before and during treatment with TORISEL.

The use of TORISEL is likely to result in hyperglycemia and hyperlipidemia. This may result in the need for

 **TORISEL**
(temsirolimus) injection
Change expectations



Please see
Prescribing
Information



Cover



Survival and 2°
End Points



Tolerability and
Safety



Predictability /
Attributes of IV



NCCN
Recommendation



Reimbursement
Support



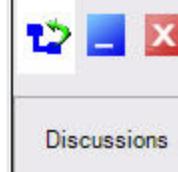
Study Design



Mechanism of
Action



Summary

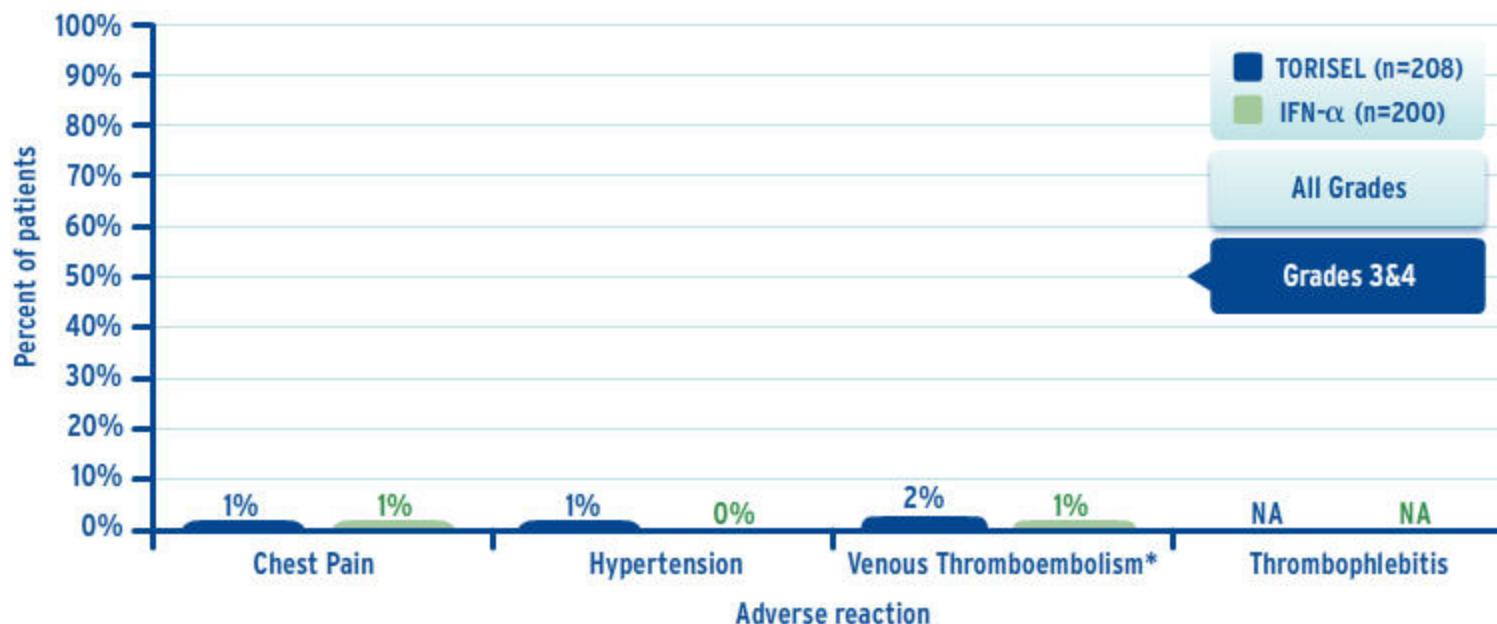


Discussions



Tolerability—Cardiovascular-related adverse reactions

Selected cardiovascular-related adverse reactions in the phase 3 trial of grades 3&4^{1,2}



Intracerebral hemorrhage

- Patients with central nervous system tumors (primary CNS tumor or metastases) and/or receiving anticoagulation therapy may be at an increased risk of developing intracerebral bleeding (including fatal outcomes) while receiving TORISEL.

*Includes deep vein thrombosis and pulmonary embolus.

Please see Important Safety Information:

- Hypersensitivity reactions manifested by symptoms, including, but not limited to anaphylaxis, dyspnea, flushing, and chest pain have been observed with TORISEL.
- Serum glucose, serum cholesterol, and triglycerides should be tested before and during treatment with TORISEL.

The use of TORISEL is likely to result in hyperglycemia and hypertension. This may result in the need for

 **TORISEL®**
(temsirolimus) injection
Change expectations

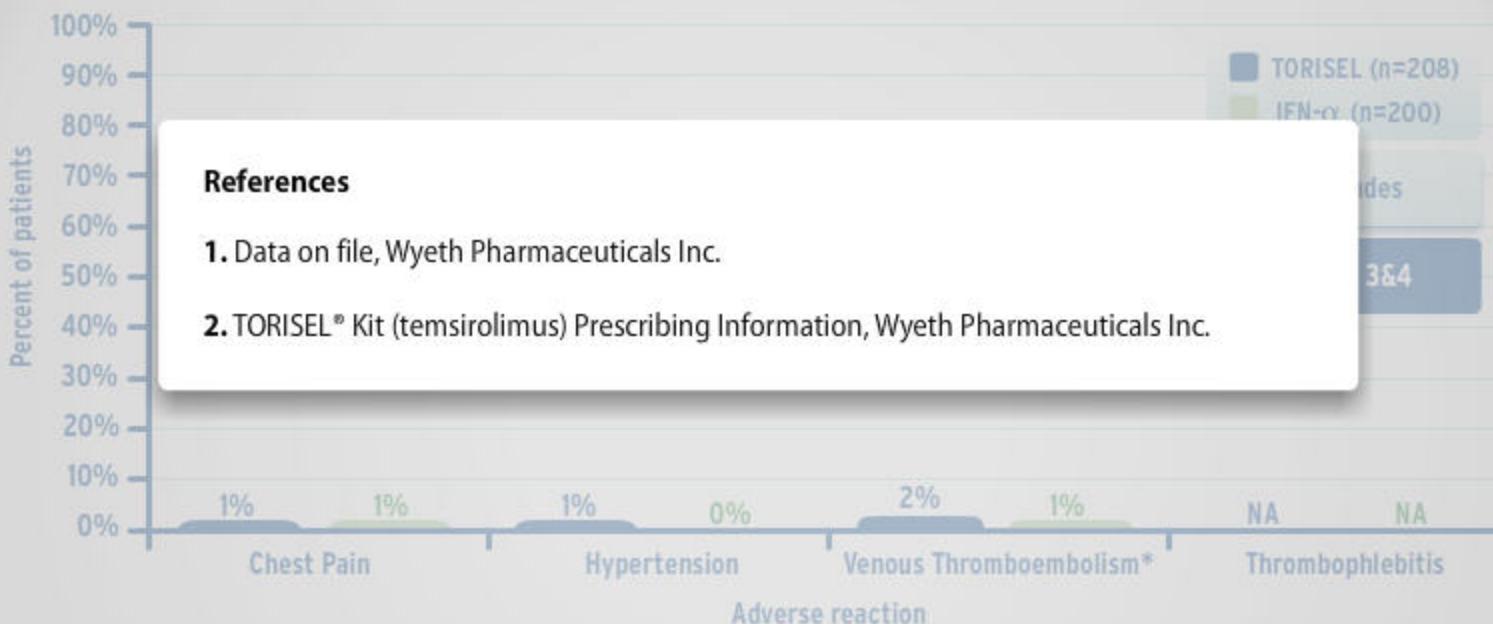


Please see
Prescribing
Information



Tolerability—Cardiovascular-related adverse reactions

Selected cardiovascular-related adverse reactions in the phase 3 trial of grades 3&4^{1,2}



References

1. Data on file, Wyeth Pharmaceuticals Inc.
2. TORISEL® Kit (temsirolimus) Prescribing Information, Wyeth Pharmaceuticals Inc.

Intracerebral hemorrhage

- Patients with central nervous system tumors (primary CNS tumor or metastases) and/or receiving anticoagulation therapy may be at an increased risk of developing intracerebral bleeding (including fatal outcomes) while receiving TORISEL.

*Includes deep vein thrombosis and pulmonary embolus.

Please see Important Safety Information:

- Hypersensitivity reactions manifested by symptoms, including, but not limited to anaphylaxis, dyspnea, flushing, and chest pain have been observed with TORISEL.
- Serum glucose, serum cholesterol, and triglycerides should be tested before and during treatment with TORISEL.

The use of TORISEL is likely to result in hyperglycemia and hyperlipidemia. This may result in the need for

 **TORISEL**
(temsirolimus) injection
Change expectations

Safety Info

Please see
Prescribing
Information



Change
expectations

Cover

S

Survival and 2nd
End Points

T

Tolerability and
Safety

P

Predictability /
Attributes of IV

NCCN

NCCN
Recommendation

Support

Reimbursement
Support

Study Design

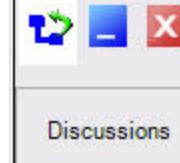
Study Design

MOA

Mechanism of
Action

Summary

Summary



Discussions



Tolerability—Laboratory abnormalities

Laboratory monitoring should be performed at the physician's discretion¹

Laboratory monitoring should be performed at the physician's discretion ¹		Grades 3&4*
Selected Laboratory Abnormalities	All Grades*	
	TORISEL 25 mg IV once weekly, n=208 (%)	IFN- α up to 18 MU 3x weekly, n=200 (%)
Any	100	98
Hematology (checked weekly)		
Chemistry (checked every 2 weeks)		

* NCI CTC Version 3.0

Please see Important Safety Information:

- Hypersensitivity reactions manifested by symptoms, including, but not limited to anaphylaxis, dyspnea, flushing, and chest pain have been observed with TORISEL.
 - Serum glucose, serum cholesterol, and triglycerides should be tested before and during treatment with TORISEL.

The use of TOPICEL® is likely to result in hyperglycemia and hyperlipidemia. This may result in the need for increased doses of insulin or oral hypoglycemic agents.



Please see
Prescribing
Information



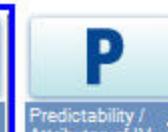
Cover



Survival and
Exit Rates



Tolerability and Safety



Predictability /



NCCN



Reimburse
Summary



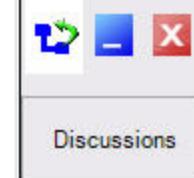
Study Design



Mechanism of Action



Summary



Discussions



Tolerability–Laboratory abnormalities

Laboratory monitoring should be performed at the physician's discretion¹

Tolerability and Safety
Planned Weekly Dose
Discontinuation Rates
Grade 3 or 4 AEs $\geq 10\%$
AEs $\geq 30\%$
Cardiovascular Information
Laboratory Abnormalities
Hypersensitivity Information
Adverse Reactions

Selected Laboratory Abnormalities	All Grades*	Grades 3&4*
	TORISEL 25 mg IV once weekly, n=208 (%)	IFN- α up to 18 MU 3x weekly, n=200 (%)
Any	78	72
Hematology (checked weekly)		
Chemistry (checked every 2 weeks)		

* NCI CTC Version 3.0.

Please see Important Safety Information:

- Hypersensitivity reactions manifested by symptoms, including, but not limited to anaphylaxis, dyspnea, flushing, and chest pain have been observed with TORISEL.
- Serum glucose, serum cholesterol, and triglycerides should be tested before and during treatment with TORISEL.

The use of TORISEL is likely to result in hyperglycemia and hyperlipidemia. This may result in the need for



	Safety Info
	Please see Prescribing Information
Cover	Survival and 2 nd End Points
	Tolerability and Safety
	Predictability / Attributes of IV
	NCCN Recommendation
	Reimbursement Support
	Study Design
	Mechanism of Action
	Summary
	Discussions



Tolerability—Laboratory abnormalities

Laboratory monitoring should be performed at the physician's discretion¹

Selected Laboratory Abnormalities		All Grades*	
		TORISEL 25 mg IV once weekly, n=208 (%)	IFN- α up to 18 MU 3x weekly, n=200 (%)
Any	Hemoglobin decreased	94	90
Hematology (checked weekly)	Lymphocytes decreased [†]	53	53
Chemistry (checked every 2 weeks)	Neutrophils decreased [†]	19	29
	Platelets decreased	40	26
	Leukocytes decreased	32	47

* NCI CTC Version 3.0.

[†] Grade 1 toxicity may be under-reported for lymphocytes and neutrophils.

Please see Important Safety Information:

- Hypersensitivity reactions manifested by symptoms, including, but not limited to anaphylaxis, dyspnea, flushing, and chest pain have been observed with TORISEL.
- Serum glucose, serum cholesterol, and triglycerides should be tested before and during treatment with TORISEL.

The use of TORISEL is likely to result in hyperglycemia and hyperlipidemia. This may result in the need for



Please see
Prescribing
Information



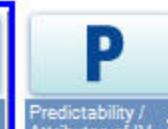
Cover



Survival and 2nd
End Points



Tolerability and
Safety



Predictability /
Attributes of IV



NCCN
Recommendation



Reimbursement
Support



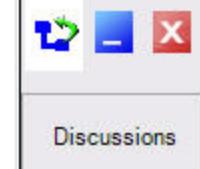
Study Design



Mechanism of
Action



Summary



Discussions



Tolerability–Laboratory abnormalities

Laboratory monitoring should be performed at the physician's discretion¹

Laboratory monitoring should be performed at the physician's discretion ¹		All Grades*	
Selected Laboratory Abnormalities		Grades 3&4*	
		TORISEL 25 mg IV once weekly, n=208 (%)	IFN- α up to 18 MU 3x weekly, n=200 (%)
Any	Hemoglobin decreased	20	22
Hematology (checked weekly)	Lymphocytes decreased [†]	16	24
Chemistry (checked every 2 weeks)	Neutrophils decreased [†]	5	10
	Platelets decreased	1	0
	Leukocytes decreased	1	6

* NCL CTC Version 3.0

[†] Grade 1 toxicity may be under-reported for lymphocytes and neutrophils.

Please see Important Safety Information:

- Hypersensitivity reactions manifested by symptoms, including, but not limited to anaphylaxis, dyspnea, flushing, and chest pain have been observed with TORISEL.
 - Serum glucose, serum cholesterol, and triglycerides should be tested before and during treatment with TORISEL.

The use of TOPICEL® is likely to result in hyperglycemia and hyperlipidemia. This may result in the need for increased doses of insulin or oral hypoglycemic agents.



Please see
Prescribing
Information



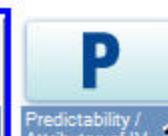
Cover



Survival analysis



Tolerability and Safety



Predictability /



NCCN



Reimbursement
Support



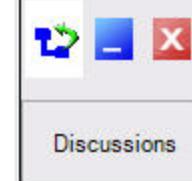
Study Design



Mechanism
Action



of Summary



Discussions



Tolerability–Laboratory abnormalities

Laboratory monitoring should be performed at the physician's discretion¹

Selected Laboratory Abnormalities		All Grades*	
		TORISEL 25 mg IV once weekly, n=208 (%)	IFN- α up to 18 MU 3x weekly, n=200 (%)
Any	Alkaline phosphatase increased	68	56
Hematology (checked weekly)	AST increased	38	52
Chemistry (checked every 2 weeks)	Creatinine increased	57	49
	Glucose increased	89	64
	Phosphorus decreased	49	31
	Total bilirubin increased	8	13
	Total cholesterol increased	87	48
	Triglycerides increased	83	72
	Potassium decreased	21	8

AST=aspartate aminotransferase

* NCI CTC Version 3.0

Please see Important Safety Information:

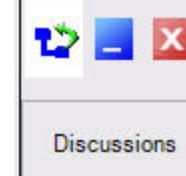
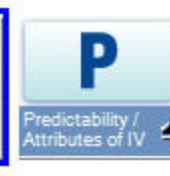
- Hypersensitivity reactions manifested by symptoms, including, but not limited to anaphylaxis, dyspnea, flushing, and chest pain have been observed with TORISEL.
 - Serum glucose, serum cholesterol, and triglycerides should be tested before and during treatment with TORISEL.

The use of TOPICEL® is likely to result in hyperglycemia and hyperlipidemia. This may result in the need for increased doses of insulin or oral hypoglycemic agents.



Safety Info

Please see
**Prescribing
Information**





Tolerability—Laboratory abnormalities

Laboratory monitoring should be performed at the physician's discretion¹

Tolerability and Safety
Planned Weekly Dose
Discontinuation Rates
Grade 3 or 4 AEs $\geq 10\%$
AEs $\geq 30\%$
Cardiovascular Information
Laboratory Abnormalities
Hypersensitivity Information
Adverse Reactions

Selected Laboratory Abnormalities	All Grades*	
	Grades 3&4*	
Any	Alkaline phosphatase increased AST increased Creatinine increased Glucose increased Phosphorus decreased Total bilirubin increased Total cholesterol increased Triglycerides increased Potassium decreased	3 2 3 16 18 1 2 44 5
Hematology (checked weekly)		7 7 1 3 9 2 1 35 0
Chemistry (checked every 2 weeks)		

AST=aspartate aminotransferase.

* NCI CTC Version 3.0.

Please see Important Safety Information:

- Hypersensitivity reactions manifested by symptoms, including, but not limited to anaphylaxis, dyspnea, flushing, and chest pain have been observed with TORISEL.
- Serum glucose, serum cholesterol, and triglycerides should be tested before and during treatment with TORISEL.

The use of TORISEL is likely to result in hyperglycemia and hyperlipidemia. This may result in the need for

 **TORISEL®**
(temsirolimus) injection
Change expectations

	Safety Info
	Please see Prescribing Information
	Cover
	Survival and 2nd End Points
	Tolerability and Safety
	Predictability / Attributes of IV
	NCCN Recommendation
	Reimbursement Support
	Study Design
	Mechanism of Action
	Summary
	Discussions



Tolerability—Laboratory abnormalities

Laboratory monitoring should be performed at the physician's discretion¹

All Grades*

Selected Laboratory Abnormalities		Grades 3&4*	
Any	Hematology	TORISEL 25 mg IV once weekly, n=208 (%)	IFN- α up to 18 MU 3x weekly, n=200 (%)
Chemistry			
		Glucose increased	10
		Phosphorus decreased	18
		Total bilirubin increased	1
		Total cholesterol increased	2
		Triglycerides increased	44
		Potassium decreased	5
			9
			2
			1
			35
			0

AST=aspartate aminotransferase.

* NCI CTC Version 3.0.

Please see Important Safety Information:

- Hypersensitivity reactions manifested by symptoms, including, but not limited to anaphylaxis, dyspnea, flushing, and chest pain have been observed with TORISEL.
- Serum glucose, serum cholesterol, and triglycerides should be tested before and during treatment with TORISEL.

The use of TORISEL is likely to result in hyperglycemia and hyperlipidemia. This may result in the need for

TORISEL
(temsirolimus) injection
Change expectations

Safety Info

Please see
Prescribing
Information





Tolerability–Hypersensitivity information

Tolerability
and Safety

Planned
Weekly Dose

Discontinuation
Rates

Grade 3 or 4
AEs ≥10%

AEs ≥30%

Cardiovascular
Information

Laboratory
Abnormalities

Hypersensitivity
Information

Adverse
Reactions



Safety
Info

Please see
Prescribing
Information

- In the phase 3 study, all hypersensitivity reactions experienced by patients receiving TORISEL alone were of Grade 1 or 2 severity¹
 - 5% of patients experienced a hypersensitivity reaction(s) on the same day as dosing, despite receiving premedication with an antihistamine¹
 - A total of 9% of patients experienced allergic or hypersensitivity reactions²
- If a patient develops a hypersensitivity reaction, stop the infusion and observe for at least 30 to 60 minutes. At the physician's discretion, treat with an H₁ antagonist, if not previously administered, and/or an H₂ antagonist. The infusion may then be resumed at a slower rate (up to 60 minutes)²
- In post-marketing surveillance, hypersensitivity reactions include some life-threatening and rare fatal reactions, which can occur very early in the first infusion of TORISEL, but may also occur with subsequent infusions. Patients should be monitored early during the infusion and appropriate supportive care should be available¹

Please see Important Safety Information:

- Hypersensitivity reactions manifested by symptoms, including, but not limited to anaphylaxis, dyspnea, flushing, and chest pain have been observed with TORISEL.
- Serum glucose, serum cholesterol, and triglycerides should be tested before and during treatment with TORISEL.

The use of TORISEL is likely to result in hyperglycemia and hyperlipidemia. This may result in the need for

TORISEL
(temsirolimus) injection
Change expectations



Tolerability–Hypersensitivity information

Tolerability
and Safety

Planned
Weekly Dose

Discontinuation
Rates

Grade 3 or 4
AEs ≥10%

AEs ≥30%

Cardiovascular
Information

Laboratory
Abnormalities

Hypersensitivity
Information

Adverse
Reactions

Safety
Info

Please see
Prescribing
Information

- In the phase 3 study, all hypersensitivity reactions experienced by patients receiving TORISEL alone were of Grade 1 or 2 severity¹
 - 5% of patients experienced a hypersensitivity reaction(s) on the same day as dosing, despite receiving a total dose of 30 to 60 mg temsirolimus administered over 6 weeks (up to 6 infusions)
- If a patient experiences a hypersensitivity reaction during treatment with TORISEL, discontinue the infusion and administer corticosteroids as appropriate.
- In post-marketing surveillance, hypersensitivity reactions include some life-threatening and rare fatal reactions, which can occur very early in the first infusion of TORISEL, but may also occur with subsequent infusions. Patients should be monitored early during the infusion and appropriate supportive care should be available¹

References

1. Data on file, Wyeth Pharmaceuticals Inc.
2. TORISEL® Kit (temsirolimus) Prescribing Information, Wyeth Pharmaceuticals Inc.

Please see Important Safety Information:

- Hypersensitivity reactions manifested by symptoms, including, but not limited to anaphylaxis, dyspnea, flushing, and chest pain have been observed with TORISEL.
- Serum glucose, serum cholesterol, and triglycerides should be tested before and during treatment with TORISEL.

The use of TORISEL is likely to result in hyperglycemia and hyperlipidemia. This may result in the need for

 **TORISEL**
(temsirolimus) injection
Change expectations




Change
expectations

Cover

S
Survival and 2nd
End Points

↑

T
Tolerability and
Safety

↓

P
Predictability /
Attributes of IV

↑

NCCN
NCCN
Recommendation

↑

Support
Reimbursement
Support

↑

Study Design
Study Design

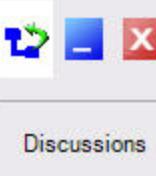
↑

MOA
Mechanism of
Action

↓

Summary
Summary

↓



Discussions



Tolerability–Adverse reactions

Adverse reactions reported in ≥10% of patients who received TORISEL or IFN- α ¹

Grades 3&4*

Adverse Reaction	All Grades*	
	TORISEL 25 mg IV once weekly, n=208 (%)	IFN- α up to 18 MU 3x weekly, n=200 (%)
Any	100	100
General disorders		
Gastrointestinal disorders		
Infections		
Musculoskeletal and connective tissue disorders		
Respiratory, thoracic, and mediastinal disorders		
Skin and subcutaneous tissue disorders		
Nervous system disorders		

* Common Toxicity Criteria for Adverse Events (CTCAE), Version 3.0.

Tolerability and Safety
Planned Weekly Dose
Discontinuation Rates
Grade 3 or 4 AEs ≥10%
AEs ≥30%
Cardiovascular Information
Laboratory Abnormalities
Hypersensitivity Information
Adverse Reactions

	Safety Info
Please see Prescribing Information	

Please see Important Safety Information:

- Hypersensitivity reactions manifested by symptoms, including, but not limited to anaphylaxis, dyspnea, flushing, and chest pain have been observed with TORISEL.
- Serum glucose, serum cholesterol, and triglycerides should be tested before and during treatment with TORISEL.

The use of TORISEL is likely to result in hyperglycemia and hyperlipidemia. This may result in the need for



	Change expectations
	Survival and 2° End Points
	Tolerability and Safety
	Predictability / Attributes of IV
	NCCN Recommendation
	Reimbursement Support
	Study Design
	Mechanism of Action
	Summary
	Discussions



Tolerability–Adverse reactions

Adverse reactions reported in ≥10% of patients who received TORISEL or IFN- α ¹

All Grades*

Adverse Reaction	Grades 3&4*	
	TORISEL 25 mg IV once weekly, n=208 (%)	IFN- α up to 18 MU 3x weekly, n=200 (%)
Any	67	78
General disorders		
Gastrointestinal disorders		
Infections		
Musculoskeletal and connective tissue disorders		
Respiratory, thoracic, and mediastinal disorders		
Skin and subcutaneous tissue disorders		
Nervous system disorders		

* Common Toxicity Criteria for Adverse Events (CTCAE), Version 3.0.

Tolerability and Safety
Planned Weekly Dose
Discontinuation Rates
Grade 3 or 4 AEs ≥10%
AEs ≥30%
Cardiovascular Information
Laboratory Abnormalities
Hypersensitivity Information
Adverse Reactions

	Safety Info
Please see Prescribing Information	

Please see Important Safety Information:

- Hypersensitivity reactions manifested by symptoms, including, but not limited to anaphylaxis, dyspnea, flushing, and chest pain have been observed with TORISEL.
- Serum glucose, serum cholesterol, and triglycerides should be tested before and during treatment with TORISEL.

The use of TORISEL is likely to result in hyperglycemia and hyperlipidemia. This may result in the need for



	Change expectations
	Survival and 2° End Points
	Tolerability and Safety
	Predictability / Attributes of IV
	NCCN Recommendation
	Reimbursement Support
	Study Design
	Mechanism of Action
	Summary
	Discussions



Tolerability–Adverse reactions

Adverse reactions reported in ≥10% of patients who received TORISEL or IFN- α ¹

Grades 3&4*

Adverse Reaction	All Grades*		
	TORISEL 25 mg IV once weekly, n=208 (%)	IFN- α up to 18 MU 3x weekly, n=200 (%)	
Any	Asthenia	51	64
General disorders	Edema [†]	35	11
Gastrointestinal disorders	Pain	28	16
Infections	Pyrexia	24	50
Musculoskeletal and connective tissue disorders	Weight loss	19	25
Respiratory, thoracic, and mediastinal disorders	Headache	15	15
Skin and subcutaneous tissue disorders	Chest pain	16	9
Nervous system disorders	Chills	8	30

* Common Toxicity Criteria for Adverse Events (CTCAE), Version 3.0.

[†] Includes edema, facial edema, and peripheral edema.

Tolerability and Safety
Planned Weekly Dose
Discontinuation Rates
Grade 3 or 4 AEs ≥10%
AEs ≥30%
Cardiovascular Information
Laboratory Abnormalities
Hypersensitivity Information
Adverse Reactions

Safety Info
Please see Prescribing Information

Please see Important Safety Information:

- Hypersensitivity reactions manifested by symptoms, including, but not limited to anaphylaxis, dyspnea, flushing, and chest pain have been observed with TORISEL.
- Serum glucose, serum cholesterol, and triglycerides should be tested before and during treatment with TORISEL.

The use of TORISEL is likely to result in hyperglycemia and hyperlipidemia. This may result in the need for



Change expectations
Cover
Survival and 2 nd End Points
Tolerability and Safety
Predictability / Attributes of IV
NCCN Recommendation
Reimbursement Support
Study Design
Mechanism of Action
Summary

Change expectations	S	T	P	NCCN	Support	Study Design	MOA	Summary	Discussions
Cover	Survival and 2 nd End Points	Tolerability and Safety	Predictability / Attributes of IV	NCCN Recommendation	Reimbursement Support	Study Design	Mechanism of Action	Summary	



Tolerability–Adverse reactions

Adverse reactions reported in ≥10% of patients who received TORISEL or IFN- α ¹

All Grades*

Adverse Reaction	Grades 3&4*		
	TORISEL 25 mg IV once weekly, n=208 (%)	IFN- α up to 18 MU 3x weekly, n=200 (%)	
Any	Asthenia Edema [†] Pain Pyrexia Weight loss Headache Chest pain Chills	11 3 5 1 1 1 1 1	26 1 2 4 2 0 1 2
General disorders			
Gastrointestinal disorders			
Infections			
Musculoskeletal and connective tissue disorders			
Respiratory, thoracic, and mediastinal disorders			
Skin and subcutaneous tissue disorders			
Nervous system disorders			

* Common Toxicity Criteria for Adverse Events (CTCAE), Version 3.0.

† Includes edema, facial edema, and peripheral edema.

Tolerability and Safety
Planned Weekly Dose
Discontinuation Rates
Grade 3 or 4 AEs ≥10%
AEs ≥30%
Cardiovascular Information
Laboratory Abnormalities
Hypersensitivity Information
Adverse Reactions

Safety Info
Please see Prescribing Information

Please see Important Safety Information:

- Hypersensitivity reactions manifested by symptoms, including, but not limited to anaphylaxis, dyspnea, flushing, and chest pain have been observed with TORISEL.
- Serum glucose, serum cholesterol, and triglycerides should be tested before and during treatment with TORISEL.

The use of TORISEL is likely to result in hyperglycemia and hyperlipidemia. This may result in the need for



Change expectations
Cover
Survival and 2 nd End Points
Tolerability and Safety
Predictability / Attributes of IV
NCCN Recommendation
Reimbursement Support
Study Design
Mechanism of Action
Summary
Discussions



Tolerability–Adverse reactions

Adverse reactions reported in ≥10% of patients who received TORISEL or IFN- α ¹

Grades 3&4*

Adverse Reaction	All Grades*		
	TORISEL 25 mg IV once weekly, n=208 (%)	IFN- α up to 18 MU 3x weekly, n=200 (%)	
Any	Mucositis [†]	41	10
General disorders	Anorexia	32	44
Gastrointestinal disorders	Nausea	37	41
Infections	Diarrhea	27	20
Musculoskeletal and connective tissue disorders	Abdominal pain	21	17
Respiratory, thoracic, and mediastinal disorders	Constipation	20	18
Skin and subcutaneous tissue disorders	Vomiting	19	29
Nervous system disorders			

* Common Toxicity Criteria for Adverse Events (CTCAE), Version 3.0.

† Includes aphthous stomatitis, glossitis, mouth ulceration, mucositis, and stomatitis.

Adverse Reactions

Safety Info

Please see Prescribing Information

Please see Important Safety Information:

- Hypersensitivity reactions manifested by symptoms, including, but not limited to anaphylaxis, dyspnea, flushing, and chest pain have been observed with TORISEL.
- Serum glucose, serum cholesterol, and triglycerides should be tested before and during treatment with TORISEL.

The use of TORISEL is likely to result in hyperglycemia and hyperlipidemia. This may result in the need for

 **TORISEL**
(temsirolimus) injection
Change expectations



Cover



Survival and 2°
End Points



Tolerability and
Safety



Predictability /
Attributes of IV



NCCN
Recommendation



Reimbursement
Support



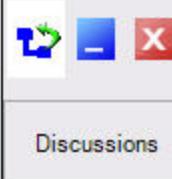
Study Design



Mechanism of
Action



Summary



Discussions



Tolerability–Adverse reactions

Adverse reactions reported in ≥10% of patients who received TORISEL or IFN- α ¹

All Grades*

Adverse Reaction	Grades 3&4*		
	TORISEL 25 mg IV once weekly, n=208 (%)	IFN- α up to 18 MU 3x weekly, n=200 (%)	
Any	Mucositis [†]	3	0
General disorders	Anorexia	3	4
Gastrointestinal disorders	Nausea	2	5
Infections	Diarrhea	1	2
Musculoskeletal and connective tissue disorders	Abdominal pain	4	2
Respiratory, thoracic, and mediastinal disorders	Constipation	0	1
Skin and subcutaneous tissue disorders	Vomiting	2	3
Nervous system disorders			

* Common Toxicity Criteria for Adverse Events (CTCAE), Version 3.0.

† Includes aphthous stomatitis, glossitis, mouth ulceration, mucositis, and stomatitis.

Tolerability and Safety
Planned Weekly Dose
Discontinuation Rates
Grade 3 or 4 AEs ≥10%
AEs ≥30%
Cardiovascular Information
Laboratory Abnormalities
Hypersensitivity Information
Adverse Reactions

Safety Info
Please see Prescribing Information

Please see Important Safety Information:

- Hypersensitivity reactions manifested by symptoms, including, but not limited to anaphylaxis, dyspnea, flushing, and chest pain have been observed with TORISEL.
- Serum glucose, serum cholesterol, and triglycerides should be tested before and during treatment with TORISEL.

The use of TORISEL is likely to result in hyperglycemia and hyperlipidemia. This may result in the need for





Tolerability–Adverse reactions

Adverse reactions reported in ≥10% of patients who received TORISEL or IFN- α ¹

Grades 3&4*

Adverse Reaction	All Grades*		
	TORISEL 25 mg IV once weekly, n=208 (%)	IFN- α up to 18 MU 3x weekly, n=200 (%)	
Any	Infections [†]	20	10
General disorders	Urinary tract infection [‡]	15	12
Gastrointestinal disorders	Pharyngitis	12	2
Infections	Rhinitis	10	2
Musculoskeletal and connective tissue disorders			
Respiratory, thoracic, and mediastinal disorders			
Skin and subcutaneous tissue disorders			
Nervous system disorders			

* Common Toxicity Criteria for Adverse Events (CTCAE), Version 3.0.

† Includes infections not otherwise specified (NOS) and the following infections that occurred infrequently as distinct entities: abscess, bronchitis, cellulitis, herpes simplex, and herpes zoster.

‡ Includes cystitis, dysuria, hematuria, urinary frequency, and urinary tract infection.

Please see Important Safety Information:

- Hypersensitivity reactions manifested by symptoms, including, but not limited to anaphylaxis, dyspnea, flushing, and chest pain have been observed with TORISEL.
- Serum glucose, serum cholesterol, and triglycerides should be tested before and during treatment with TORISEL.

The use of TORISEL is likely to result in hyperglycemia and hyperlipidemia. This may result in the need for

 **TORISEL®**
(temsirolimus) injection
Change expectations



Please see
Prescribing
Information





Tolerability–Adverse reactions

Adverse reactions reported in ≥10% of patients who received TORISEL or IFN- α ¹

All Grades*

Adverse Reaction	Grades 3&4*		
	TORISEL 25 mg IV once weekly, n=208 (%)	IFN- α up to 18 MU 3x weekly, n=200 (%)	
Any	Infections [†]	3	2
General disorders	Urinary tract infection [‡]	1	2
Gastrointestinal disorders	Pharyngitis	0	0
Infections	Rhinitis	0	0
Musculoskeletal and connective tissue disorders			
Respiratory, thoracic, and mediastinal disorders			
Skin and subcutaneous tissue disorders			
Nervous system disorders			

* Common Toxicity Criteria for Adverse Events (CTCAE), Version 3.0.

† Includes infections not otherwise specified (NOS) and the following infections that occurred infrequently as distinct entities: abscess, bronchitis, cellulitis, herpes simplex, and herpes zoster.

‡ Includes cystitis, dysuria, hematuria, urinary frequency, and urinary tract infection.

Please see Important Safety Information:

- Hypersensitivity reactions manifested by symptoms, including, but not limited to anaphylaxis, dyspnea, flushing, and chest pain have been observed with TORISEL.
- Serum glucose, serum cholesterol, and triglycerides should be tested before and during treatment with TORISEL.

The use of TORISEL is likely to result in hyperglycemia and hyperlipidemia. This may result in the need for

 **TORISEL®**
(temsirolimus) injection
Change expectations



Please see
Prescribing
Information



Cover



Survival and 2°
End Points



Tolerability and
Safety



Predictability /
Attributes of IV



NCCN
Recommendation



Reimbursement
Support



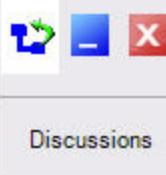
Study Design



Mechanism of
Action



Summary



Discussions



Tolerability–Adverse reactions

Adverse reactions reported in ≥10% of patients who received TORISEL or IFN- α ¹

Grades 3&4*

Adverse Reaction	All Grades*	
	TORISEL 25 mg IV once weekly, n=208 (%)	IFN- α up to 18 MU 3x weekly, n=200 (%)
Any	Back pain Arthralgia Myalgia	20 18 8
General disorders		
Gastrointestinal disorders		
Infections		
Musculoskeletal and connective tissue disorders		
Respiratory, thoracic, and mediastinal disorders		
Skin and subcutaneous tissue disorders		
Nervous system disorders		

* Common Toxicity Criteria for Adverse Events (CTCAE), Version 3.0.

- Tolerability and Safety
- Planned Weekly Dose
- Discontinuation Rates
- Grade 3 or 4 AEs ≥10%
- AEs ≥30%
- Cardiovascular Information
- Laboratory Abnormalities
- Hypersensitivity Information
- Adverse Reactions

- Safety Info
- Please see Prescribing Information

Please see Important Safety Information:

- Hypersensitivity reactions manifested by symptoms, including, but not limited to anaphylaxis, dyspnea, flushing, and chest pain have been observed with TORISEL.
- Serum glucose, serum cholesterol, and triglycerides should be tested before and during treatment with TORISEL.

The use of TORISEL is likely to result in hyperglycemia and hyperlipidemia. This may result in the need for

 **TORISEL**
(temsirolimus) injection
Change expectations



Tolerability–Adverse reactions

Adverse reactions reported in ≥10% of patients who received TORISEL or IFN- α ¹

All Grades*

Adverse Reaction	Grades 3&4*	
	TORISEL 25 mg IV once weekly, n=208 (%)	IFN- α up to 18 MU 3x weekly, n=200 (%)
Any	Back pain 3	4
General disorders	Arthralgia 1	1
Gastrointestinal disorders	Myalgia 1	1
Infections		
Musculoskeletal and connective tissue disorders		
Respiratory, thoracic, and mediastinal disorders		
Skin and subcutaneous tissue disorders		
Nervous system disorders		

* Common Toxicity Criteria for Adverse Events (CTCAE), Version 3.0.

Tolerability and Safety
Planned Weekly Dose
Discontinuation Rates
Grade 3 or 4 AEs ≥10%
AEs ≥30%
Cardiovascular Information
Laboratory Abnormalities
Hypersensitivity Information
Adverse Reactions

	Safety Info
Please see Prescribing Information	

Please see Important Safety Information:

- Hypersensitivity reactions manifested by symptoms, including, but not limited to anaphylaxis, dyspnea, flushing, and chest pain have been observed with TORISEL.
- Serum glucose, serum cholesterol, and triglycerides should be tested before and during treatment with TORISEL.

The use of TORISEL is likely to result in hyperglycemia and hyperlipidemia. This may result in the need for



Change expectations	S	T	P	NCCN	Support	Study Design	MOA	Summary	Discussions
Cover	Survival and 2 nd End Points	Tolerability and Safety	Predictability / Attributes of IV	NCCN Recommendation	Reimbursement Support	Study Design	Mechanism of Action	Summary	Discussions



Tolerability–Adverse reactions

Adverse reactions reported in ≥10% of patients who received TORISEL or IFN- α ¹

Grades 3&4*

Adverse Reaction	All Grades*	
	TORISEL 25 mg IV once weekly, n=208 (%)	IFN- α up to 18 MU 3x weekly, n=200 (%)
Any	Dyspnea 28	Epistaxis 24
General disorders	Cough 26	
Gastrointestinal disorders		4
Infections		
Musculoskeletal and connective tissue disorders		
Respiratory, thoracic, and mediastinal disorders		
Skin and subcutaneous tissue disorders		
Nervous system disorders		

* Common Toxicity Criteria for Adverse Events (CTCAE), Version 3.0.

Adverse Reactions

Safety Info

Please see Prescribing Information

Please see Important Safety Information:

- Hypersensitivity reactions manifested by symptoms, including, but not limited to anaphylaxis, dyspnea, flushing, and chest pain have been observed with TORISEL.
- Serum glucose, serum cholesterol, and triglycerides should be tested before and during treatment with TORISEL.

The use of TORISEL is likely to result in hyperglycemia and hyperlipidemia. This may result in the need for

 **TORISEL**
(temsirolimus) injection
Change expectations



Tolerability–Adverse reactions

Adverse reactions reported in ≥10% of patients who received TORISEL or IFN- α ¹

All Grades*

Adverse Reaction	Grades 3&4*	
	TORISEL 25 mg IV once weekly, n=208 (%)	IFN- α up to 18 MU 3x weekly, n=200 (%)
Any	Dyspnea 9	Epistaxis 6
General disorders	Cough 1	0
Gastrointestinal disorders	Epistaxis 0	0
Infections		
Musculoskeletal and connective tissue disorders		
Respiratory, thoracic, and mediastinal disorders		
Skin and subcutaneous tissue disorders		
Nervous system disorders		

* Common Toxicity Criteria for Adverse Events (CTCAE), Version 3.0.

- Tolerability and Safety
- Planned Weekly Dose
- Discontinuation Rates
- Grade 3 or 4 AEs ≥10%
- AEs ≥30%
- Cardiovascular Information
- Laboratory Abnormalities
- Hypersensitivity Information
- Adverse Reactions

- Safety Info
- Please see Prescribing Information

Please see Important Safety Information:

- Hypersensitivity reactions manifested by symptoms, including, but not limited to anaphylaxis, dyspnea, flushing, and chest pain have been observed with TORISEL.
- Serum glucose, serum cholesterol, and triglycerides should be tested before and during treatment with TORISEL.

The use of TORISEL is likely to result in hyperglycemia and hyperlipidemia. This may result in the need for

 **TORISEL**
(temsirolimus) injection
Change expectations



Tolerability–Adverse reactions

Adverse reactions reported in ≥10% of patients who received TORISEL or IFN- α ¹

Grades 3&4*

Adverse Reaction	All Grades*		
	TORISEL 25 mg IV once weekly, n=208 (%)	IFN- α up to 18 MU 3x weekly, n=200 (%)	
Any	Rash [†]	47	7
General disorders	Pruritus	19	8
Gastrointestinal disorders	Nail disorder	14	1
Infections	Dry skin	11	7
Musculoskeletal and connective tissue disorders	Acne	10	1
Respiratory, thoracic, and mediastinal disorders			
Skin and subcutaneous tissue disorders			
Nervous system disorders			

* Common Toxicity Criteria for Adverse Events (CTCAE), Version 3.0.

† Includes eczema, exfoliative dermatitis, maculopapular rash, pruritic rash, pustular rash, rash (NOS), and vesiculobullous rash.

Adverse Reactions

Safety Info

Please see Prescribing Information



Please see Important Safety Information:

- Hypersensitivity reactions manifested by symptoms, including, but not limited to anaphylaxis, dyspnea, flushing, and chest pain have been observed with TORISEL.
- Serum glucose, serum cholesterol, and triglycerides should be tested before and during treatment with TORISEL.

The use of TORISEL is likely to result in hyperglycemia and hyperlipidemia. This may result in the need for

TORISEL
(temsirolimus) injection
Change expectations



Cover



Survival and 2°
End Points



Tolerability and
Safety



Predictability /
Attributes of IV



NCCN
Recommendation



Reimbursement
Support



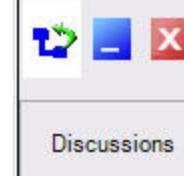
Study Design



Mechanism of
Action



Summary



Discussions



Tolerability–Adverse reactions

Adverse reactions reported in ≥10% of patients who received TORISEL or IFN- α ¹

All Grades*

Adverse Reaction	Grades 3&4*		
	TORISEL 25 mg IV once weekly, n=208 (%)	IFN- α up to 18 MU 3x weekly, n=200 (%)	
Any	Rash [†]	5	0
General disorders	Pruritus	1	0
Gastrointestinal disorders	Nail disorder	0	0
Infections	Dry skin	1	0
Musculoskeletal and connective tissue disorders	Acne	0	0
Respiratory, thoracic, and mediastinal disorders			
Skin and subcutaneous tissue disorders			
Nervous system disorders			

* Common Toxicity Criteria for Adverse Events (CTCAE), Version 3.0.

† Includes eczema, exfoliative dermatitis, maculopapular rash, pruritic rash, pustular rash, rash (NOS), and vesiculobullous rash.

Adverse Reactions

Safety Info

Please see Prescribing Information



Please see Important Safety Information:

- Hypersensitivity reactions manifested by symptoms, including, but not limited to anaphylaxis, dyspnea, flushing, and chest pain have been observed with TORISEL.
- Serum glucose, serum cholesterol, and triglycerides should be tested before and during treatment with TORISEL.

The use of TORISEL is likely to result in hyperglycemia and hyperlipidemia. This may result in the need for

TORISEL
(temsirolimus) injection
Change expectations



Cover



Survival and 2°
End Points



Tolerability and
Safety



Predictability /
Attributes of IV



NCCN
Recommendation



Reimbursement
Support



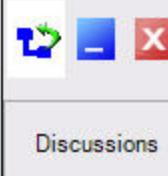
Study Design



Mechanism of
Action



Summary



Discussions



Tolerability
and Safety

Planned
Weekly Dose

Discontinuation
Rates

Grade 3 or 4
AEs ≥10%

AEs ≥30%

Cardiovascular
Information

Laboratory
Abnormalities

Hypersensitivity
Information

Adverse
Reactions



Safety
Info

Please see
Prescribing
Information



Pruritic Rash



Pruritic Maculopapular Rash

Courtesy of the Cleveland Clinic Taussig Cancer Institute

Nervous system disorders

* Common Toxicity Criteria for Adverse Events (CTCAE), Version 3.0.

† Includes eczema, exfoliative dermatitis, maculopapular rash, pruritic rash, pustular rash, rash (NOS), and vesiculobullous rash.

Please see Important Safety Information:

- Hypersensitivity reactions manifested by symptoms, including, but not limited to anaphylaxis, dyspnea, flushing, and chest pain have been observed with TORISEL.
- Serum glucose, serum cholesterol, and triglycerides should be tested before and during treatment with TORISEL.

The use of TORISEL is likely to result in hyperglycemia and hyperlipidemia. This may result in the need for

TORISEL
(temsirolimus) injection
Change expectations



Cover



Survival and 2°
End Points



Tolerability and
Safety



Predictability /
Attributes of IV



NCCN
Recommendation



Reimbursement
Support



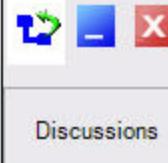
Study Design



Mechanism of
Action



Summary



Discussions



Tolerability–Adverse reactions

Adverse reactions reported in ≥10% of patients who received TORISEL or IFN- α ¹

Grades 3&4*

Adverse Reaction	All Grades*		
	TORISEL 25 mg IV once weekly, n=208 (%)	IFN- α up to 18 MU 3x weekly, n=200 (%)	
Any	Dysgeusia [†]	20	9
General disorders	Insomnia	12	15
Gastrointestinal disorders	Depression	4	14
Infections			
Musculoskeletal and connective tissue disorders			
Respiratory, thoracic, and mediastinal disorders			
Skin and subcutaneous tissue disorders			
Nervous system disorders			

* Common Toxicity Criteria for Adverse Events (CTCAE), Version 3.0.

† Includes taste loss and taste perversion.

Adverse Reactions



Safety Info

Please see
Prescribing
Information

Please see Important Safety Information:

- Hypersensitivity reactions manifested by symptoms, including, but not limited to anaphylaxis, dyspnea, flushing, and chest pain have been observed with TORISEL.
- Serum glucose, serum cholesterol, and triglycerides should be tested before and during treatment with TORISEL.

The use of TORISEL is likely to result in hyperglycemia and hyperlipidemia. This may result in the need for

TORISEL
(temsirolimus) injection
Change expectations



Tolerability–Adverse reactions

Adverse reactions reported in ≥10% of patients who received TORISEL or IFN- α ¹

All Grades*

Adverse Reaction	Grades 3&4*	
	TORISEL 25 mg IV once weekly, n=208 (%)	IFN- α up to 18 MU 3x weekly, n=200 (%)
Any	Dysgeusia [†] 0	0
General disorders	Insomnia 1	0
Gastrointestinal disorders	Depression 0	2
Infections		
Musculoskeletal and connective tissue disorders		
Respiratory, thoracic, and mediastinal disorders		
Skin and subcutaneous tissue disorders		
Nervous system disorders		

* Common Toxicity Criteria for Adverse Events (CTCAE), Version 3.0.

† Includes taste loss and taste perversion.

- Tolerability and Safety
- Planned Weekly Dose
- Discontinuation Rates
- Grade 3 or 4 AEs ≥10%
- AEs ≥30%
- Cardiovascular Information
- Laboratory Abnormalities
- Hypersensitivity Information
- Adverse Reactions

- Safety Info
- Please see Prescribing Information

Please see Important Safety Information:

- Hypersensitivity reactions manifested by symptoms, including, but not limited to anaphylaxis, dyspnea, flushing, and chest pain have been observed with TORISEL.
- Serum glucose, serum cholesterol, and triglycerides should be tested before and during treatment with TORISEL.

The use of TORISEL is likely to result in hyperglycemia and hyperlipidemia. This may result in the need for

 **TORISEL®**
(temsirolimus) injection
Change expectations



Tolerability–Adverse reactions

Adverse reactions reported in ≥10% of patients who received TORISEL or IFN- α [†]

All Grades*

Adverse Reaction	Grades 3&4*	
	TORISEL 25 mg IV	IFN- α up to 18 MU
Any		
General disorders and administration site conditions		
Gastrointestinal disorders		
Infections and infestations		
Musculoskeletal and connective tissue disorders		
Respiratory, thoracic, and mediastinal disorders		
Skin and subcutaneous tissue disorders		
Nervous system disorders		

References

1. TORISEL® Kit (temsirolimus) Prescribing Information, Wyeth Pharmaceuticals Inc.
2. Data on file, Wyeth Pharmaceuticals Inc.

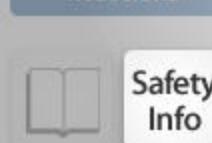
* Common Toxicity Criteria for Adverse Events (CTCAE), Version 3.0.
† Includes taste loss and taste perversion.

Please see Important Safety Information:

- Hypersensitivity reactions manifested by symptoms, including, but not limited to anaphylaxis, dyspnea, flushing, and chest pain have been observed with TORISEL.
- Serum glucose, serum cholesterol, and triglycerides should be tested before and during treatment with TORISEL.

The use of TORISEL is likely to result in hyperglycemia and hyperlipidemia. This may result in the need for

TORISEL
(temsirolimus) injection
Change expectations



Please see
Prescribing
Information





Predictability and Attributes of IV

Predictable Dose Delivery

Attributes of Administration

TORISEL—The first and only IV mTOR inhibitor indicated for advanced RCC¹

Predictable dose delivery with IV administration^{1,2}

Controlled and accurate drug delivery

- TORISEL is administered as a weekly 25 mg IV infusion¹
- TORISEL typically achieves peak exposure and 100% bioavailability by the end of the infusion (30-60 minutes)^{1,2}

TORISEL: Predictable concentrations over each treatment cycle^{3*†}

- Temsirolimus initial median peak concentration of 572.7 ng/mL (25th, 75th percentile: 510.5, 642.3) was achieved by the end of the infusion, and the median trough level prior to the next infusion was 0.05 ng/mL (25th, 75th percentile: 0.02, 0.13)^{3†}
- The principal metabolite (sirolimus) median peak concentration was 64.2 ng/mL (25th, 75th percentile: 42.5, 93.1) and the median trough level was 4.6 ng/mL (25th, 75th percentile: 1.96, 12.1)³

CYP3A interactions

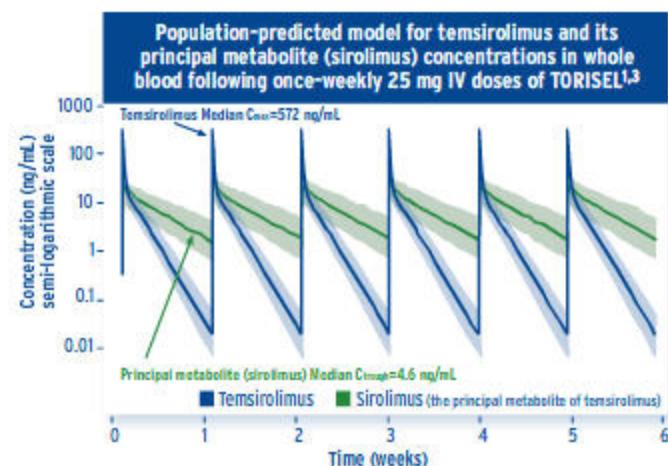
- Strong inducers of CYP3A4/5 (eg, dexamethasone, rifampin) and strong inhibitors of CYP3A4 (eg, ketoconazole, atazanavir) may decrease and increase concentrations of the major metabolite of TORISEL, respectively. If alternatives cannot be used, dose modifications of TORISEL are recommended.
- St. John's Wort may decrease TORISEL plasma concentrations, and grapefruit juice may increase plasma concentrations of the major metabolite of TORISEL, and therefore both should be avoided.

Please see Section 2 in the full Prescribing Information for complete Dosage and Administration Information.

Please see Important Safety Information:

- Hypersensitivity reactions manifested by symptoms, including, but not limited to anaphylaxis, dyspnea, flushing, and chest pain have been observed with TORISEL.
- Serum glucose, serum cholesterol, and triglycerides should be tested before and during treatment with TORISEL.

The use of TORISEL is likely to result in hyperglycemia and hyperlipidemia. This may result in the need for



* Based on population-predicted data across multiple clinical trials following once-weekly TORISEL 25 mg IV infusion. Whole blood concentrations of temsirolimus were based on 1153 observations from 90 subjects, 49 of whom had advanced RCC. Whole blood concentrations of the principal metabolite of temsirolimus (sirolimus) were based on 1312 observations from 211 subjects, 107 of whom had advanced RCC.³

Following administration of a single 25 mg dose of TORISEL in patients with cancer, mean temsirolimus C_{max} in whole blood was 585 ng/mL (coefficient of variation, CV=14%).¹

† The clinical relevance of this information is unknown.



Please see
Prescribing
Information



Change
expectations

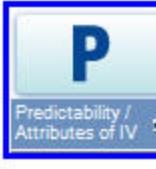
Cover



Survival and 2°
End Points



Tolerability and
Safety



Predictability /
Attributes of IV



NCCN
Recommendation



Support



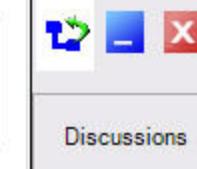
Study Design



MOA



Summary



Discussions



Predictability and Attributes of IV

Predictable Dose Delivery

Attributes of Administration

TORISEL—The first and only IV mTOR inhibitor indicated for advanced RCC¹

Predictable dose delivery with IV administration^{1,2}

Controlled and accurate drug delivery

- TORISEL is administered as a weekly 25 mg IV infusion¹
- TORISEL typically achieves peak exposure and 100% bioavailability by the end of the infusion (30-60 minutes)^{1,2}

TORISEL: Predictable concentrations over each treatment cycle^{3*†}

- Temsirolimus initial median peak concentration of 572.7 ng/mL (25th, 75th percentile: 510.5, 642.3) was achieved by the end of the infusion, and the median trough level prior to the next infusion was 0.05 ng/mL (25th, 75th percentile: 0.02, 0.13)^{3†}
- The principal metabolite (sirolimus) median peak concentration was 64.2 ng/mL (25th, 75th percentile: 42.5, 93.1) and the median trough level was 4.6 ng/mL (25th, 75th percentile: 1.96, 12.1)³

CYP3A interactions

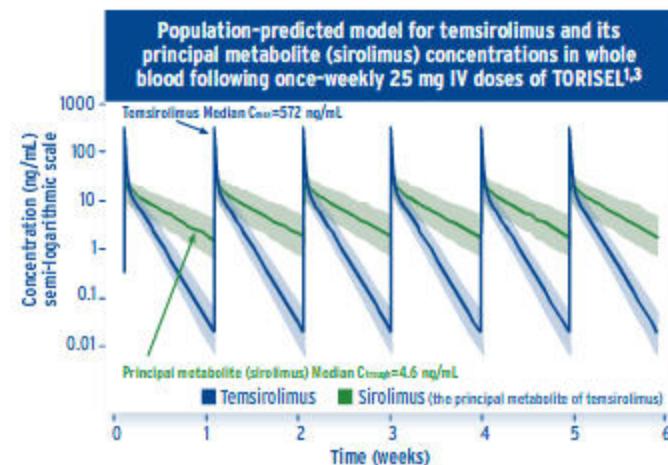
- Strong inducers of CYP3A4/5 (eg, dexamethasone, rifampin) and strong inhibitors of CYP3A4 (eg, ketoconazole, atazanavir) may decrease and increase concentrations of the major metabolite of TORISEL, respectively. If alternatives cannot be used, dose modifications of TORISEL are recommended.
- St. John's Wort may decrease TORISEL plasma concentrations, and grapefruit juice may increase plasma concentrations of the major metabolite of TORISEL, and therefore both should be avoided.

Please see Section 2 in the full Prescribing Information for complete Dosage and Administration Information.

Please see Important Safety Information:

- Hypersensitivity reactions manifested by symptoms, including, but not limited to anaphylaxis, dyspnea, flushing, and chest pain have been observed with TORISEL.
- Serum glucose, serum cholesterol, and triglycerides should be tested before and during treatment with TORISEL.

The use of TORISEL is likely to result in hyperglycemia and hyperlipidemia. This may result in the need for



* Based on population-predicted data across multiple clinical trials following once-weekly TORISEL 25 mg IV infusion. Whole blood concentrations of temsirolimus were based on 1153 observations from 90 subjects, 49 of whom had advanced RCC. Whole blood concentrations of the principal metabolite of temsirolimus (sirolimus) were based on 1312 observations from 211 subjects, 107 of whom had advanced RCC.³

Following administration of a single 25 mg dose of TORISEL in patients with cancer, mean temsirolimus C_{max} in whole blood was 585 ng/mL (coefficient of variation, CV=14%).¹

† The clinical relevance of this information is unknown.



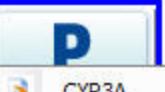
Cover



Survival and 2nd End Points



Tolerability and Safety



CYP3A
Attributes of IV



Recommendation



Reimbursement Support



Study Design



Mechanism of Action



Summary



Discussions



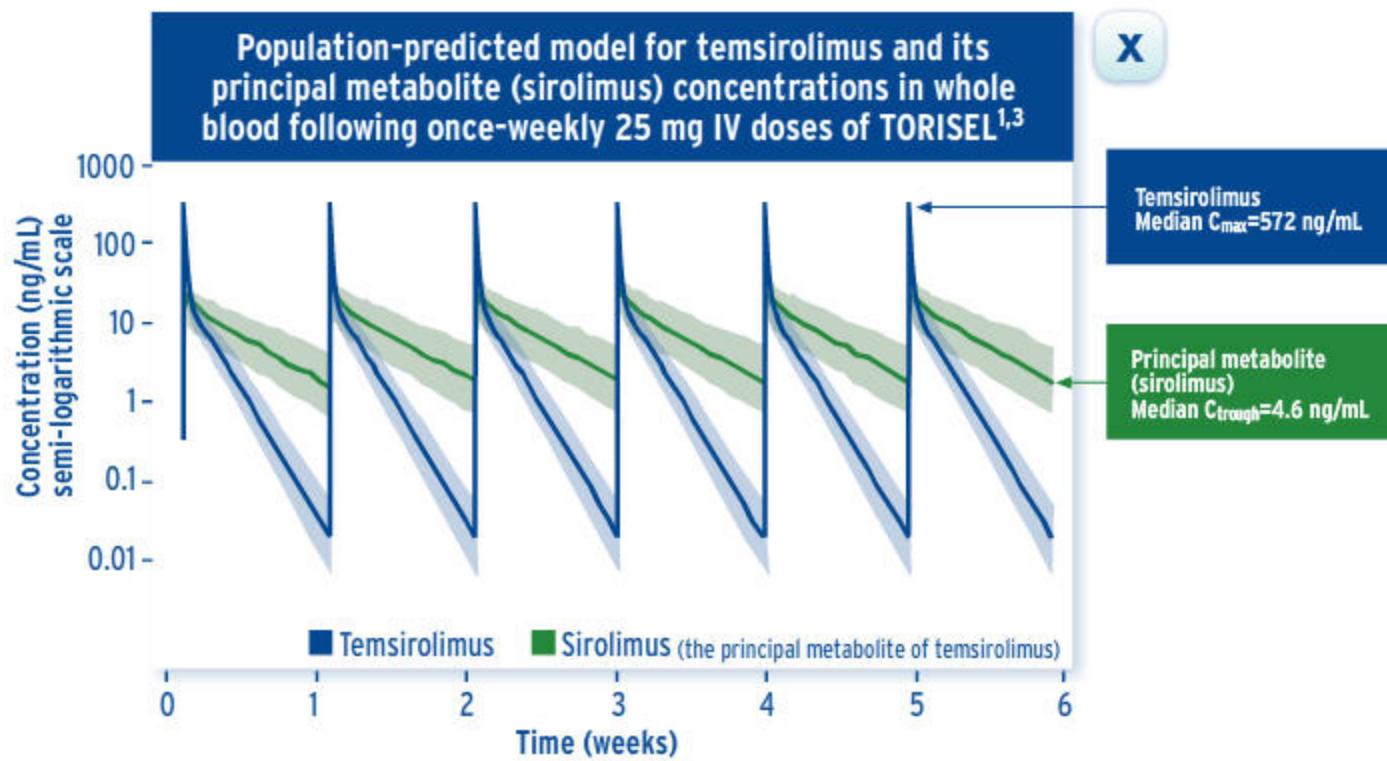
TORISEL®—The first and only IV mTOR inhibitor indicated for advanced RCC¹

Predictable dose delivery with IV administration^{1,2}

Predictability and Attributes of IV

Predictable Dose Delivery

Attributes of Administration



Please see Important Safety Information:

- Hypersensitivity reactions manifested by symptoms, including, but not limited to anaphylaxis, dyspnea, flushing, and chest pain have been observed with TORISEL.
- Serum glucose, serum cholesterol, and triglycerides should be tested before and during treatment with TORISEL.

The use of TORISEL is likely to result in hyperglycemia and hyperlipidemia. This may result in the need for

TORISEL®
(temsirolimus) injection
Change expectations



Safety Info

Please see Prescribing Information



Cover



Survival and 2nd End Points



Tolerability and Safety



Predictability / Attributes of IV



NCCN Recommendation



Reimbursement Support



Study Design



Mechanism of Action



Summary



Discussions



TORISEL®—The first and only IV mTOR inhibitor indicated for advanced RCC¹

Predictable dose delivery with IV administration^{1,2}

Predictability and Attributes of IV

Controlled and accurate drug delivery

- TORISEL is administered as a weekly 25 mg IV infusion¹

• T

TO

• T

• T

• T

• T

• T

• T

• T

• T

• T

• T

• T

• T

• T

• T

• T

• T

• T

• T

• T

• T

• T

• T

• T

• T

• T

• T

• T

• T

• T

• T

• T

• T

• T

• T

• T

• T

• T

• T

• T

• T

• T

• T

• T

• T

• T

• T

• T

• T

• T

• T

• T

• T

• T

• T

• T

• T

• T

• T

• T

• T

• T

• T

• T

• T

• T

• T

• T

• T

• T

• T

• T

• T

• T

• T

• T

• T

• T

• T

• T

• T

• T

• T

• T

• T

• T

• T

• T

• T

• T

• T

• T

• T

• T

• T

• T

• T

• T

• T

• T

• T

• T

• T

• T

• T

• T

• T

• T

• T

• T

• T

• T

• T

• T

• T

• T

• T

• T

• T

• T

• T

• T

• T

• T

• T

• T

• T

• T

• T

• T

• T

• T

• T

• T

• T

• T

• T

• T

• T

• T

• T

• T

• T

• T

• T

• T

• T

• T

• T

• T

• T

• T

• T

• T

• T

• T

• T

• T

• T

• T

• T

• T

• T

• T

• T

• T

• T

• T

• T

• T

• T

• T

• T

• T

• T

• T

• T

• T

• T

• T

• T

• T

• T

• T

• T

• T

• T

• T

• T

• T

• T

• T

• T

• T

• T

• T

• T

• T

• T

• T

• T

• T

• T

• T

• T

• T

• T

• T

• T

• T

• T

• T

• T

• T

• T

• T

• T

• T

• T

• T

• T

• T

• T

• T

• T

• T

• T

• T

• T

• T

• T

• T

• T

• T

• T

• T

• T

• T

• T

• T

• T

• T

• T

• T

• T

• T

• T

• T

• T

• T

• T

• T

• T

• T

• T

• T

• T

• T

• T

• T

• T

• T

• T

• T

• T

• T

• T

• T

• T

• T

• T

• T

• T

• T

• T

• T

• T

• T

• T

• T

• T

• T

• T

• T

• T

• T

• T

• T

• T

• T

• T

• T

• T

• T

• T

• T

• T

• T

• T

• T

• T

• T



Attributes of IV administration of TORISEL

Predictability and Attributes of IV

Predictable Dose Delivery

Attributes of Administration

Provides opportunities for patient monitoring

- Enables physician monitoring of dose adherence¹
- Enables weekly monitoring for possible adverse reactions
- Provides opportunities for patient education¹

Bioavailability is not affected by¹

- GI function
- Food intake



Hypersensitivity information

- Patients should receive prophylactic intravenous diphenhydramine 25 to 50 mg (or similar antihistamine) approximately 30 minutes before the start of each dose of TORISEL²
- If a patient develops a hypersensitivity reaction, stop the infusion and observe for at least 30 to 60 minutes. At the physician's discretion, treat with an H₁ antagonist, if not previously administered, and/or an H₂ antagonist. The infusion may then be resumed at a slower rate (up to 60 minutes)²
 - Hypersensitivity reactions, some life-threatening, can occur early in the first infusion, or during subsequent infusions³
 - Patients should be monitored early during the infusion and appropriate supportive care should be available

Please see Section 2 in the full Prescribing Information for complete Dosage and Administration information.



Safety Info

Please see Prescribing Information

Please see Important Safety Information:

- Hypersensitivity reactions manifested by symptoms, including, but not limited to anaphylaxis, dyspnea, flushing, and chest pain have been observed with TORISEL.
- Serum glucose, serum cholesterol, and triglycerides should be tested before and during treatment with TORISEL.

The use of TORISEL is likely to result in hyperglycemia and hyperlipidemia. This may result in the need for

 **TORISEL**
(temsirolimus) injection
Change expectations



Change expectations

Cover

S

Survival and 2nd End Points

T

Tolerability and Safety

P

Predictability / Attributes of IV

NCCN

NCCN Recommendation

Support

Reimbursement Support

Study Design

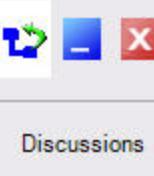
Study Design

MOA

Mechanism of Action

Summary

Summary



Discussions

Attributes of IV administration of TORISEL

Provides opportunities for patient monitoring

- Enables physician monitoring of dose adherence¹

Hypersensitivity information

- Patients should receive nonhylaric intravenous diphendydramine 25 to

References

1. Weingart SN, Brown E, Bach PB, et al. NCCN task force report: oral chemotherapy. *J Natl Compr Canc Netw.* 2008;6(suppl 3):S-1–S-14.
2. TORISEL® Kit (temsirolimus) Prescribing Information, Wyeth Pharmaceuticals Inc.
3. Data on file, Wyeth Pharmaceuticals Inc.



supportive care should be available

Please see Section 2 in the full Prescribing Information for complete Dosage and Administration information.

Safety Info

Please see Prescribing Information

Please see Important Safety Information:

- Hypersensitivity reactions manifested by symptoms, including, but not limited to anaphylaxis, dyspnea, flushing, and chest pain have been observed with TORISEL.
- Serum glucose, serum cholesterol, and triglycerides should be tested before and during treatment with TORISEL.

The use of TORISEL is likely to result in hyperglycemia and hyperlipidemia. This may result in the need for

TORISEL
(temsirolimus) injection
Change expectations



Cover



Survival and 2° End Points



Tolerability and Safety



Predictability / Attributes of IV



NCCN Recommendation



Reimbursement Support



Study Design



Mechanism of Action



Summary



Discussions



NCCN recommends TORISEL as a first- and second-line treatment option in advanced RCC¹

TORISEL is the only IV mTOR inhibitor indicated for advanced RCC²

TORISEL first line

- The NCCN recommends TORISEL as a first-line treatment option¹

TORISEL second line

- The NCCN recommends TORISEL as a second-line treatment option¹

NCCN=National Comprehensive Cancer Network.

Please see Important Safety Information:

- Hypersensitivity reactions manifested by symptoms, including, but not limited to anaphylaxis, dyspnea, flushing, and chest pain have been observed with TORISEL.
- Serum glucose, serum cholesterol, and triglycerides should be tested before and during treatment with TORISEL.

The use of TORISEL is likely to result in hyperglycemia and hyperlipidemia. This may result in the need for



 **TORISEL®**
(temsirolimus) injection
Change expectations



Safety
Info

Please see
Prescribing
Information



Cover



Survival and 2nd
End Points



Tolerability and
Safety



Predictability /
Attributes of IV



NCCN
Recommendation



Reimbursement
Support



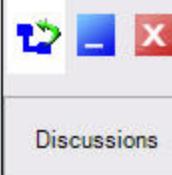
Study Design



Mechanism of
Action



Summary



Discussions

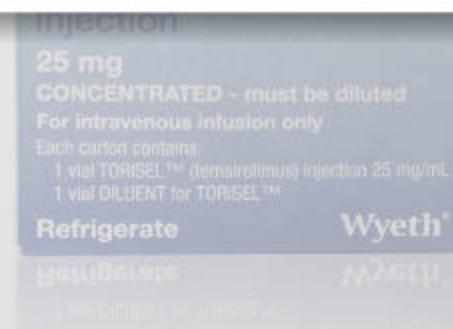


NCCN recommends TORISEL as a first- and second-line treatment option in advanced RCC¹

TORISEL is the only IV mTOR inhibitor indicated for advanced RCC²

References

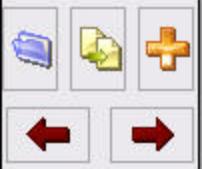
1. TORISEL® Kit (temsirolimus) Prescribing Information, Wyeth Pharmaceuticals Inc.
2. National Comprehensive Cancer Network. NCCN clinical practice guidelines in oncology: kidney cancer. V.2.2009.



NCCN=National Comprehensive Cancer Network.

Safety Info

Please see
Prescribing
Information



Please see Important Safety Information:

- Hypersensitivity reactions manifested by symptoms, including, but not limited to anaphylaxis, dyspnea, flushing, and chest pain have been observed with TORISEL.
- Serum glucose, serum cholesterol, and triglycerides should be tested before and during treatment with TORISEL.

The use of TORISEL is likely to result in hyperglycemia and hyperlipidemia. This may result in the need for

TORISEL
(temsirolimus) injection
Change expectations



Cover



Survival and 2°
End Points



Tolerability and
Safety



Predictability /
Attributes of IV



NCCN
Recommendation



Support



Study Design



MOA



Summary



Discussions



Reimbursement
Support

Comprehensive reimbursement support with a single phone call

Dedicated personnel nationwide

- Easy access to a wide variety of reimbursement services
 - Identification of TORISEL coverage policy for federal, state, and private payers
 - Recommendation of alternatives for patients with inadequate or no coverage
 - Comprehensive prior authorization support
 - Claims tracking assistance
 - Claims denial appeal assistance

TORISEL Patient Assistance Program

- For eligible patients who lack adequate coverage

Hints for the CMS 1500 Form

Please see Important Safety Information:

- Hypersensitivity reactions manifested by symptoms, including, but not limited to anaphylaxis, dyspnea, flushing, and chest pain have been observed with TORISEL.
- Serum glucose, serum cholesterol, and triglycerides should be tested before and during treatment with TORISEL.

The use of TORISEL is likely to result in hyperglycemia and hyperlipidemia. This may result in the need for

J-Code Specific for TORISEL

J9330 - Injection, temsirolimus
NDC Code: 0008-1179-01

1 mg of TORISEL = 1 billable unit

1 TORISEL kit = 25 billable units

**Call 1-866-WYETH-ONC
(1-866-993-8466)**

Monday through Friday, 9 a.m. to 6 p.m. ET, to speak to your dedicated Regional Reimbursement Consultant.

Easy access to reimbursement forms at www.TORISEL.com



Safety
Info

Please see
Prescribing
Information



Cover



Survival and 2nd End Points



Tolerability and Safety



Predictability / Attributes of IV



NCCN Recommendation



Reimbursement Support



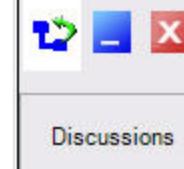
Study Design



Mechanism of Action



Summary



Discussions



Reimbursement
Support

Comprehensive reimbursement support with a single phone call

Dedicated personnel nationwide

- Easy access to a wide variety of reimbursement services
 - Identification of TORISEL coverage policy for federal, state, and private payers
 - Recommendation of alternatives for patients with inadequate or no coverage
 - Comprehensive prior authorization support
 - Claims tracking assistance
 - Claims denial appeal assistance

TORISEL Patient Assistance Program

- For eligible patients who lack adequate coverage

Hints for the CMS 1500 Form

Please see Important Safety Information:

- Hypersensitivity reactions manifested by symptoms, including, but not limited to anaphylaxis, dyspnea, flushing, and chest pain have been observed with TORISEL.
- Serum glucose, serum cholesterol, and triglycerides should be tested before and during treatment with TORISEL.

The use of TORISEL is likely to result in hyperglycemia and hyperlipidemia. This may result in the need for

J-Code Specific for TORISEL

J9330 - Injection, temsirolimus
NDC Code: 0008-1179-01

1 mg of TORISEL = 1 billable unit

1 TORISEL kit = 25 billable units

**Call 1-866-WYETH-ONC
(1-866-993-8466)**

Monday through Friday, 9 a.m. to 6 p.m. ET, to speak to your dedicated Regional Reimbursement Consultant.

Easy access to reimbursement forms at www.TORISEL.com

Safety
Info

Please see
Prescribing
Information

**TORISEL**
(temsirolimus) injection
Change expectations



Cover



Survival and 2nd
End Points



Tolerability and
Safety



Predictability /
Attributes of IV



NCCN
Recommendation



J Code Form
Support



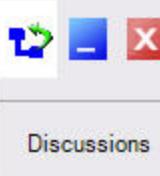
Study
Design



Mechanism of
Action



Summary



Discussions



TORISEL® Studied as first-line therapy in advanced RCC^{1,2}

Patient randomization in the first-line phase 3 study

Study Design

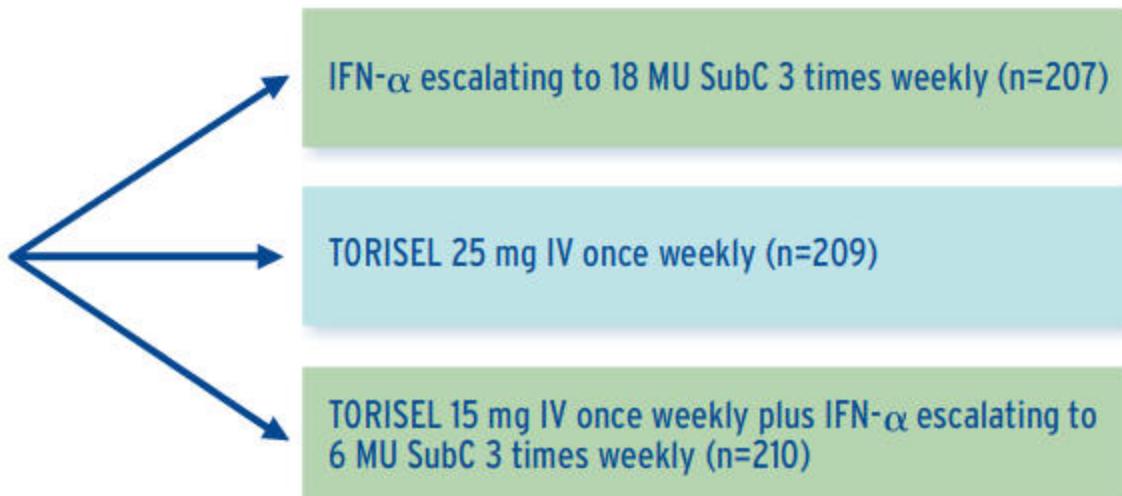
Randomization

Disease Characteristics

Risk Factors

**RANDOMIZED
(N=626)**

Stratified by geographic region and nephrectomy¹



Treatment with the combination of TORISEL 15 mg and IFN- α was associated with an increased incidence of multiple adverse reactions and did not result in a significant increase in OS when compared with IFN- α alone.¹



Safety Info

Please see Prescribing Information

Please see Important Safety Information:

- Hypersensitivity reactions manifested by symptoms, including, but not limited to anaphylaxis, dyspnea, flushing, and chest pain have been observed with TORISEL.
- Serum glucose, serum cholesterol, and triglycerides should be tested before and during treatment with TORISEL.

The use of TORISEL is likely to result in hyperglycemia and hyperlipidemia. This may result in the need for

TORISEL®
(temsirolimus) injection
Change expectations



Cover



Survival and 2nd End Points



Tolerability and Safety



Predictability / Attributes of IV



NCCN Recommendation



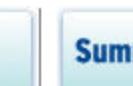
Reimbursement Support



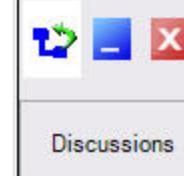
Study Design



Mechanism of Action



Summary



Discussions



TORISEL® Studied as first-line therapy in advanced RCC^{1,2}

Patient randomization in the first-line phase 3 study

Study Design

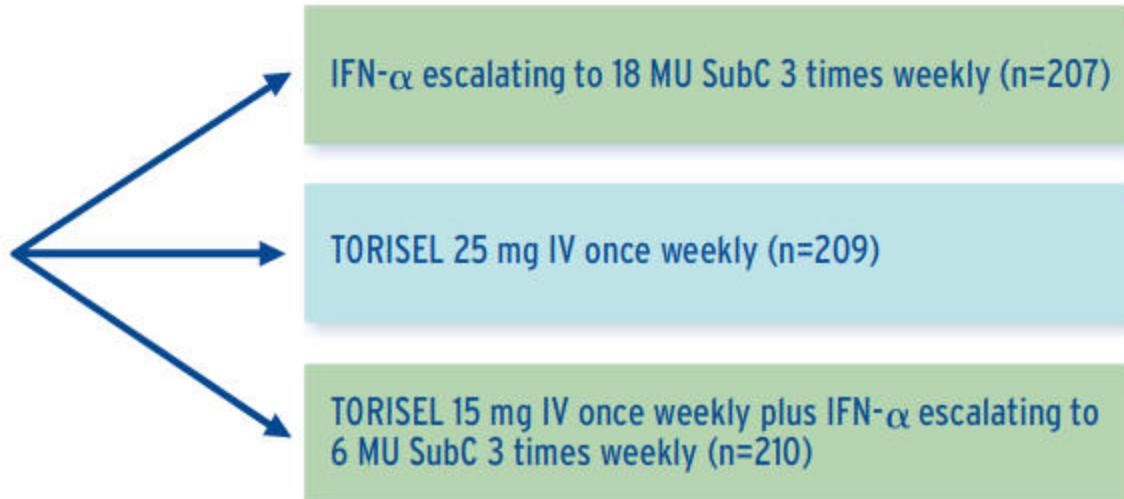
Randomization

Disease
Characteristics

Risk Factors

**RANDOMIZED
(N=626)**

Stratified by geographic
region and nephrectomy¹



Treatment with the combination of TORISEL 15 mg and IFN- α was associated with an increased incidence of multiple adverse reactions and did not result in a significant increase in OS when compared with IFN- α alone.¹

Safety
Info

Please see
Prescribing
Information

Please see Important Safety Information:

- Hypersensitivity reactions manifested by symptoms, including, but not limited to anaphylaxis, dyspnea, flushing, and chest pain have been observed with TORISEL.
- Serum glucose, serum cholesterol, and triglycerides should be tested before and during treatment with TORISEL.

The use of TORISEL is likely to result in hyperglycemia and hyperlipidemia. This may result in the need for

TORISEL®
(temsirolimus) injection
Change expectations



Change
expectations

Cover

S

Survival and 2nd
End Points

T

Tolerability and
Safety

P

Predictability /
Attributes of IV

NCCN

NCCN
Recommendation

Support

Reimbursement
Support

**Study
Design**

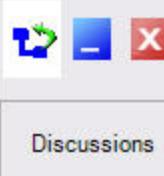
Hudes Reprint

MOA

Action

Summary

Summary



Discussions



TORISEL® Studied as first-line therapy in advanced RCC^{1,2}

Patient randomization in the first-line phase 3 study

Study Design

Randomization

Disease
Characteristics

Risk Factors

RAN
(N)

Stratified
region an

References

1. TORISEL® Kit (temsirolimus) Prescribing Information, Wyeth Pharmaceuticals Inc.
2. Data on file, Wyeth Pharmaceuticals Inc.

IFN- α escalating to 18 MU SubC 3 times weekly (n=207)

TORISEL 15 mg IV once weekly plus IFN- α escalating to 6 MU SubC 3 times weekly (n=210)

Treatment with the combination of TORISEL 15 mg and IFN- α was associated with an increased incidence of multiple adverse reactions and did not result in a significant increase in OS when compared with IFN- α alone.¹

Safety
Info

Please see
Prescribing
Information

Please see Important Safety Information:

- Hypersensitivity reactions manifested by symptoms, including, but not limited to anaphylaxis, dyspnea, flushing, and chest pain have been observed with TORISEL.
- Serum glucose, serum cholesterol, and triglycerides should be tested before and during treatment with TORISEL.

The use of TORISEL is likely to result in hyperglycemia and hyperlipidemia. This may result in the need for

TORISEL
(temsirolimus) injection
Change expectations



Change
expectations

Cover

S

Survival and 2nd
End Points

T

Tolerability and
Safety

P

Predictability /
Attributes of IV

NCCN

NCCN
Recommendation

Support

Reimbursement
Support

**Study
Design**

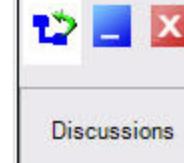
Study Design

MOA

Mechanism of
Action

Summary

Summary



Discussions



TORISEL® Studied as first-line therapy in advanced RCC^{1,2}

Patient randomization in the first-line phase 3 study

Study Design
Randomization
Disease Characteristics
Risk Factors

Disease Characteristics ^{2,3}		
Characteristic	TORISEL 25 mg (n=209)	IFN- α up to 18 MU 3x weekly (n=207)
<u>Primary cell type</u>		
Clear	80.9%	82.1%
Other	19.1%	17.9%
<u>Prior nephrectomy</u>		
No	33.5%	32.9%
Yes	66.5%	67.1%

	Safety Info
Please see Prescribing Information	

Please see Important Safety Information:

- Hypersensitivity reactions manifested by symptoms, including, but not limited to anaphylaxis, dyspnea, flushing, and chest pain have been observed with TORISEL.
- Serum glucose, serum cholesterol, and triglycerides should be tested before and during treatment with TORISEL.

The use of TORISEL is likely to result in hyperglycemia and hyperlipidemia. This may result in the need for



			Change expectations	S	T	P	NCCN	Support	Study Design	MOA	Summary			
Cover	Survival and 2 nd End Points	Tolerability and Safety	Predictability / Attributes of IV	NCCN Recommendation	Reimbursement Support	Study Design	Mechanism of Action	Summary	Discussions					



TORISEL

Patient ran...

Study Design

Randomization

Disease
Characteristics

Risk Factors

Character...

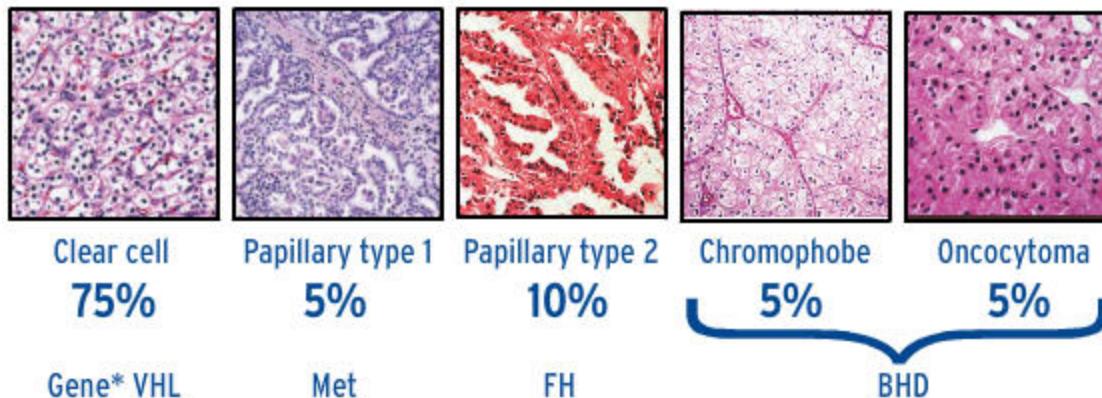
Primary

Clear
Other

Prior ne...

No
Yes

5 Different Histologies of RCC and Their Incidence⁴



*von Hippel-Lindau (VHL) is a hereditary form of clear cell renal carcinoma. Hereditary papillary renal carcinoma, Met allele, is a hereditary form of papillary renal carcinoma (papillary type 1). Papillary type 2, fumarate hydrase (FH), is a hereditary form of renal cell carcinoma. Birt Hogg Dubé (BHD) is a hereditary form of chromophobe and oncocytoma of renal cell carcinoma.

Used with permission from Linehan WM, Walther MM, Zbar B. The genetic basis of cancer of the kidney. *J Urol.* 2003;170:2163-2172.

Safety
InfoPlease see
Prescribing
Information

Please see Important Safety Information:

- Hypersensitivity reactions manifested by symptoms, including, but not limited to anaphylaxis, dyspnea, flushing, and chest pain have been observed with TORISEL.
- Serum glucose, serum cholesterol, and triglycerides should be tested before and during treatment with TORISEL.

The use of TORISEL is likely to result in hyperglycemia and hypertension. This may result in the need for...

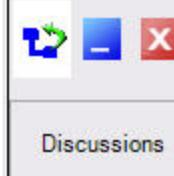
TORISEL
(temsirolimus) injection
Change expectations



Cover

Survival and 2nd
End PointsTolerability and
SafetyPredictability /
Attributes of IVNCCN
RecommendationReimbursement
SupportStudy
DesignMechanism of
Action

Summary



Discussions



TORISEL® Studied as first-line therapy in advanced RCC^{1,2}

Patient randomization in the first-line phase 3 study

Study Design

Randomization

Disease
Characteristics

Risk Factors

References

1. TORISEL® Kit (temsirolimus) Prescribing Information, Wyeth Pharmaceuticals Inc.
2. Data on file, Wyeth Pharmaceuticals Inc.
3. Hudes G, Carducci M, Tomczak P, et al. Temsirolimus, interferon alfa, or both for advanced renal-cell carcinoma. *N Engl J Med.* 2007;356:2271-2281.
4. Linehan WM, Walther MM, Zbar B. The genetic basis of cancer of the kidney. *J Urol.* 2003;170:2163-2172.

Prior nephrectomy

No	33.5%	32.9%
Yes	66.5%	67.1%

Safety
Info

Please see
Prescribing
Information

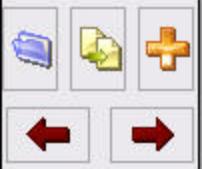
Please see Important Safety Information:

- Hypersensitivity reactions manifested by symptoms, including, but not limited to anaphylaxis, dyspnea, flushing, and chest pain have been observed with TORISEL.
- Serum glucose, serum cholesterol, and triglycerides should be tested before and during treatment with TORISEL.

The use of TORISEL® is likely to result in hyperglycemia and hyperlipidemia. This may result in the need for



TORISEL
(temsirolimus) injection
Change expectations



Change
expectations

Cover

S

Survival and 2nd
End Points

T

Tolerability and
Safety

P

Predictability /
Attributes of IV

NCCN

NCCN
Recommendation

Support

Reimbursement
Support

**Study
Design**

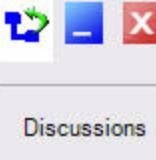
Study Design

MOA

Mechanism of
Action

Summary

Summary



Discussions



TORISEL is indicated for patients with advanced RCC

Studied as first-line treatment in patients with ≥ 3 of 6 preselected prognostic risk factors¹

Preselected Prognostic Risk Factors

(based on modified MSKCC criteria)¹⁻⁴

<u>MSKCC criteria</u>	<u>Additional risk factor</u>
<ul style="list-style-type: none"> Karnofsky performance status (KPS) <80 <ul style="list-style-type: none"> In the phase 3 study, patients were required to have a KPS of 60 or 70* Hemoglobin less than the lower limit of normal <1 year from time of initial RCC diagnosis to randomization Corrected calcium >10 mg/dL Lactate dehydrogenase >1.5 times the upper limit of normal 	<ul style="list-style-type: none"> >1 metastatic organ site

MSKCC=Memorial Sloan-Kettering Cancer Center.

* Karnofsky performance status of 60 indicates the patient requires occasional assistance, but is able to care for most of his or her needs.
Karnofsky performance status of 70 indicates the patient cares for himself or herself, but is unable to carry on normal activity or do active work.

Most patients (94%) had ≥ 3 of 6 prognostic risk factors at randomization.²

Please see Important Safety Information:

- Hypersensitivity reactions manifested by symptoms, including, but not limited to anaphylaxis, dyspnea, flushing, and chest pain have been observed with TORISEL.
- Serum glucose, serum cholesterol, and triglycerides should be tested before and during treatment with TORISEL.

The use of TORISEL is likely to result in hyperglycemia and hyperlipidemia. This may result in the need for

 **TORISEL**
(temsirolimus) injection
Change expectations


Safety Info


Please see Prescribing Information





Cover



Survival and 2nd End Points



Tolerability and Safety



Predictability / Attributes of IV



NCCN Recommendation



Reimbursement Support



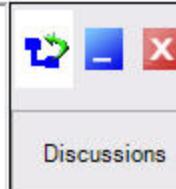
Study Design



Mechanism of Action



Summary



Discussions



TORISEL® is indicated for patients with advanced RCC.

Impact of the Number of MSKCC Risk Factors on Patient Outcomes^{3*}

No. of Risk Factors	Risk Groups	% of Patients	Median OS
3 or more	Poor	20%	4.9 months
1 or 2	Intermediate	62%	13.8 months
0	Favorable	18%	29.6 months

OS=overall survival.

- >2 years difference in median OS between poor and favorable patients³
- Significant differences in OS across the 3 risk groups ($P<0.0001$)³

*Retrospective analysis of 463 patients with advanced RCC receiving IFN- α as first-line systemic therapy in 6 prospective clinical trials.³

MSKCC=Memorial Sloan-Kettering Cancer Center.

* Karnofsky performance status of 60 indicates the patient requires occasional assistance, but is able to care for most of his or her needs.

Karnofsky performance status of 70 indicates the patient cares for himself or herself, but is unable to carry on normal activity or do active work.

Most patients (94%) had ≥ 3 of 6 prognostic risk factors at randomization.²

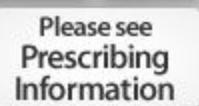
Please see Important Safety Information:

- Hypersensitivity reactions manifested by symptoms, including, but not limited to anaphylaxis, dyspnea, flushing, and chest pain have been observed with TORISEL.
- Serum glucose, serum cholesterol, and triglycerides should be tested before and during treatment with TORISEL.

The use of TORISEL® is likely to result in hyperglycemia and hyperlipidemia. This may result in the need for



Safety
Info



Please see
Prescribing
Information



Cover



Survival and 2°
End Points



Tolerability and
Safety



Predictability /
Attributes of IV



NCCN
Recommendation



Reimbursement
Support



Study Design



Mechanism of
Action



Summary



Discussions



TORISEL is indicated for patients with advanced RCC

Impact of the Number of CCF Risk Factors on Patient Outcomes^{5*}

No. of Risk Factors	Risk Groups	% of Patients	Median OS
3 or more	Poor	28%	7.3 months
2	Intermediate	35%	14.4 months
0 or 1	Favorable	37%	26.0 months

CCF = Cleveland Clinic Foundation

*Retrospective analysis of phase 1 and phase 2 studies in which a total of 353 patients (308 analyzed) received investigational agents or combination therapies as first-line treatment for metastatic RCC.⁵

MSKCC=Memorial Sloan-Kettering Cancer Center.

* Karnofsky performance status of 60 indicates the patient requires occasional assistance, but is able to care for most of his or her needs. Karnofsky performance status of 70 indicates the patient cares for himself or herself, but is unable to carry on normal activity or do active work.

Most patients (94%) had ≥3 of 6 prognostic risk factors at randomization.²

Please see Important Safety Information:

- Hypersensitivity reactions manifested by symptoms, including, but not limited to anaphylaxis, dyspnea, flushing, and chest pain have been observed with TORISEL.
- Serum glucose, serum cholesterol, and triglycerides should be tested before and during treatment with TORISEL.

The use of TORISEL is likely to result in hyperglycemia and hyperlipidemia. This may result in the need for



Safety Info

Please see Prescribing Information



Cover



Survival and 2nd End Points



Tolerability and Safety



Predictability / Attributes of IV



NCCN Recommendation



Reimbursement Support



Study Design



Mechanism of Action



Summary



Discussions



TORISEL is indicated for patients with advanced RCC

Studied

References

1. TORISEL® Kit (temsirolimus) Prescribing Information, Wyeth Pharmaceuticals Inc.
2. Data on file, Wyeth Pharmaceuticals Inc.
3. Motzer RJ, Bacik J, Murphy BA, et al. Interferon-alfa as a comparative treatment for clinical trials of new therapies against advanced renal cell carcinoma. *J Clin Oncol.* 2002;20:289-296.
4. Gerber LH, Vargo MM, Smith RG. Rehabilitation of the cancer patient. In: DeVita VT Jr, Hellman S, Rosenberg SA, eds. *Cancer Principles and Practice of Oncology*. 7th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2005:2719-2746.
5. Mekhail TM, Abou-Jawde RM, BouMerhi G, et al. Validation and extension of the Memorial Sloan-Kettering prognostic factors model for survival in patients with previously untreated metastatic renal cell carcinoma. *J Clin Oncol.* 2005;23:832-841.

MSKCC=Memorial Sloan-Kettering Cancer Center.

- * Karnofsky performance status of 60 indicates the patient requires occasional assistance, but is able to care for most of his or her needs.
- Karnofsky performance status of 70 indicates the patient cares for himself or herself, but is unable to carry on normal activity or do active work.

Most patients (94%) had ≥ 3 of 6 prognostic risk factors at randomization.²

Safety Info

Please see Important Safety Information:

- Hypersensitivity reactions manifested by symptoms, including, but not limited to anaphylaxis, dyspnea, flushing, and chest pain have been observed with TORISEL.
- Serum glucose, serum cholesterol, and triglycerides should be tested before and during treatment with TORISEL.

The use of TORISEL is likely to result in hyperglycemia and hyperlipidemia. This may result in the need for



Cover



Survival and 2nd End Points



Tolerability and Safety



Predictability / Attributes of IV



NCCN Recommendation



Reimbursement Support



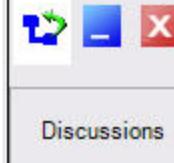
Study Design



Mechanism of Action



Summary



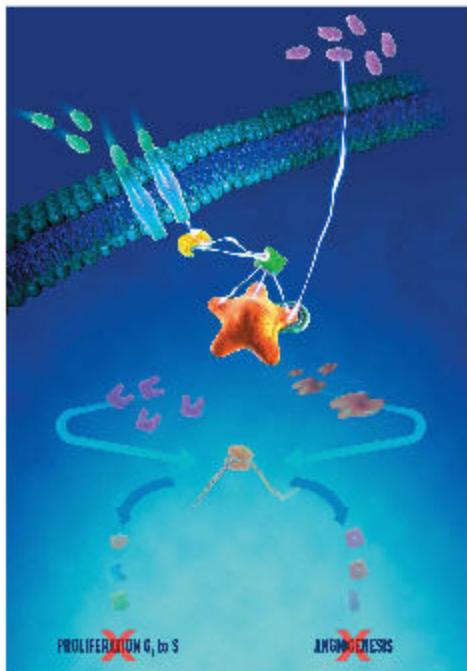
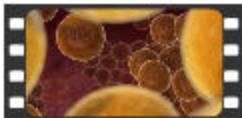
Discussions

 **TORISEL**
(temsirolimus) injection
Change expectations



TORISEL—The first mTOR inhibitor approved for advanced renal cell carcinoma (RCC)¹

TORISEL induces anti-proliferative and anti-angiogenic activity by inhibiting mTOR¹⁻⁴



mTOR=mammalian target of rapamycin



Safety
Info

Please see
Prescribing
Information

Please see Important Safety Information:

- Hypersensitivity reactions manifested by symptoms, including, but not limited to anaphylaxis, dyspnea, flushing, and chest pain have been observed with TORISEL.
- Serum glucose, serum cholesterol, and triglycerides should be tested before and during treatment with TORISEL.

The use of TORISEL is likely to result in hyperglycemia and hyperlipidemia. This may result in the need for

 **TORISEL®**
(temsirolimus) injection



Cover



Survival and 2°
End Points



Tolerability and
Safety



Predictability /
Attributes of IV



NCCN
Recommendation



Reimbursement
Support



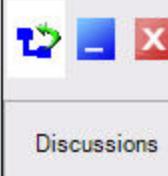
Study Design



Mechanism of
Action



Summary

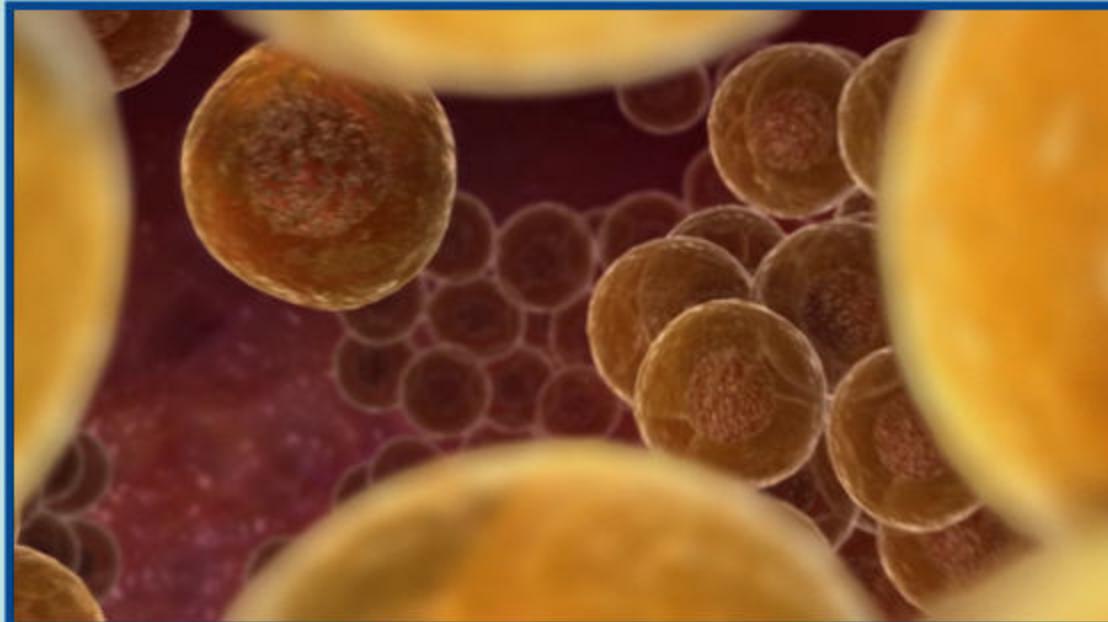


Discussions



TORI

TORISE

noma (RCC)¹

mTOR=mammalian target of rapamycin

Safety
InfoPlease see
Prescribing
Information**Please see Important Safety Information:**

- Hypersensitivity reactions manifested by symptoms, including, but not limited to anaphylaxis, dyspnea, flushing, and chest pain have been observed with TORISEL.
- Serum glucose, serum cholesterol, and triglycerides should be tested before and during treatment with TORISEL.

The use of TORISEL is likely to result in hyperglycemia and hyperlipidemia. This may result in the need for
TORISEL
(temsirolimus) injection

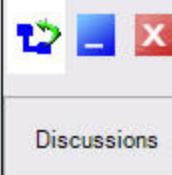
Cover

Survival and 2nd
End PointsTolerability and
SafetyPredictability /
Attributes of IVNCCN
RecommendationReimbursement
Support

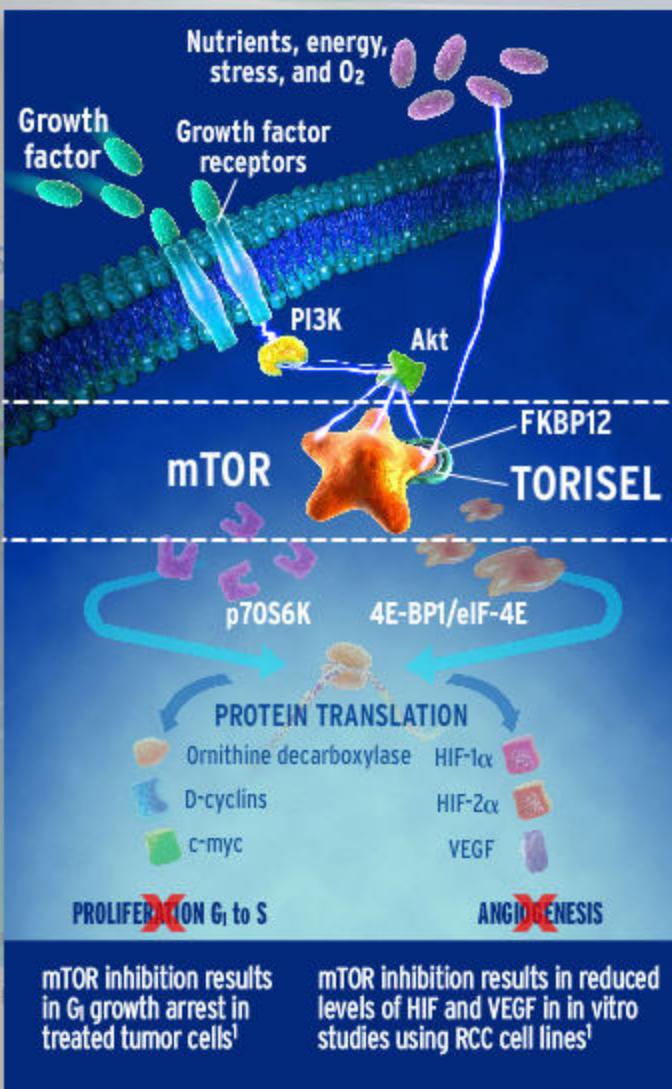
Study Design

Mechanism of
Action

Summary



Discussions



UPSTREAM PATHWAY^{2,3}

TORISEL INHIBITS mTOR¹⁻³

TORISEL binds to the intracellular protein FKBP12, and the resulting complex binds to and inhibits mTOR¹

DOWNSTREAM PATHWAY^{2,3}

The inhibition of mTOR blocks 2 downstream pathways—p70S6K and 4E-BP1¹⁻³

mTOR=mammalian target of rapamycin

HIF=hypoxia-inducible factor

VEGF=vascular endothelial growth factor

Please see Important Safety Information:

- Hypersensitivity reactions manifested by symptoms, including, but not limited to anaphylaxis, dyspnea, flushing, and chest pain have been observed with TORISEL.
- Serum glucose, serum cholesterol, and triglycerides should be tested before and during treatment with TORISEL.

The use of TORISEL is likely to result in hyperglycemia and hyperlipidemia. This may result in the need for

TORISEL
(temsirolimus) injection

Safety Info

Please see
Prescribing
Information



Cover



Survival and 2nd End Points



Tolerability and Safety



Predictability / Attributes of IV



NCCN Recommendation



Reimbursement Support



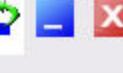
Study Design



Mechanism of Action



Summary



Discussions



TORISEL®—The first mTOR inhibitor approved for advanced renal cell carcinoma (RCC)¹

TORISEL induces anti-proliferative and anti-angiogenic activity by inhibiting mTOR¹⁻⁴



References

1. TORISEL® Kit (temsirolimus) Prescribing Information, Wyeth Pharmaceuticals Inc.
2. Abraham RT, Gibbons JJ. The mammalian target of rapamycin signaling pathway: twists and turns in the road to cancer therapy. *Clin Cancer Res.* 2007;13:3109-3114.
3. Adjei AA, Hidalgo M. Intracellular signal transduction pathway proteins as targets for cancer therapy. *J Clin Oncol.* 2005;23:5386-5403.
4. Huang S, Houghton PJ. Targeting mTOR signaling for cancer therapy. *Curr Opin Pharmacol.* 2003;3:371-377.



mTOR=mammalian target of rapamycin

Safety Info

Please see
Prescribing
Information



Please see Important Safety Information:

- Hypersensitivity reactions manifested by symptoms, including, but not limited to anaphylaxis, dyspnea, flushing, and chest pain have been observed with TORISEL.
- Serum glucose, serum cholesterol, and triglycerides should be tested before and during treatment with TORISEL.

The use of TORISEL is likely to result in hyperglycemia and hyperlipidemia. This may result in the need for

TORISEL
(temsirolimus) injection



Cover



Survival and 2nd End Points



Tolerability and Safety



Predictability / Attributes of IV



NCCN Recommendation



Reimbursement Support



Study Design



Mechanism of Action



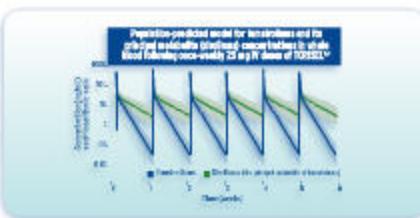
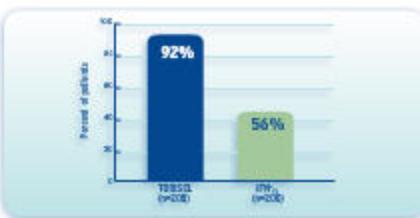
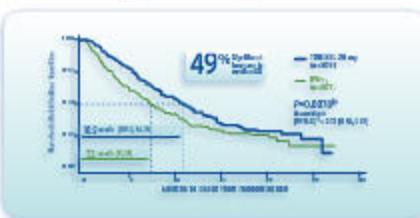
Summary



Discussions



TORISEL®—The first and only IV mTOR inhibitor indicated for advanced RCC¹ Change expectations with TORISEL



Overall survival benefit achieved as first-line therapy

- 49% significant increase in median OS compared with IFN- α ($P=0.0078^*$)
(Hazard Ratio [95% CI][†] = 0.73 [0.58, 0.92])
-10.9 months [8.6, 12.7] vs. 7.3 months [6.1, 8.8], respectively¹

Planned weekly dose and common AEs

- 92% of the planned weekly dose of TORISEL was received on average²
- The most common ($\geq 10\%$) Grade 3/4 adverse reactions and laboratory abnormalities were hypertriglyceridemia (44%), anemia (20%), hypophosphatemia (18%), lymphopenia (16%), hyperglycemia (16%), and asthenia (11%)¹

Predictable dose delivery and attributes of IV administration

- IV dosing facilitates controlled and accurate drug delivery³
 - Peak exposure typically occurred by the end of the infusion (30-60 minutes)¹
 - 100% bioavailability³
- Weekly IV administration provides monitoring opportunities
 - Enables physician monitoring of dose adherence⁴
 - Enables weekly monitoring for possible adverse reactions

* A comparison is considered statistically significant if the P -value is <0.0159 (O'Brien-Fleming boundary at 446 deaths).

[†] Based on Cox proportional hazard model stratified by prior nephrectomy and region.

Wyeth®

© 2009, Wyeth Pharmaceuticals Inc., Philadelphia, PA 19101

September 2009

253629-01



Safety
Info

Please see
Prescribing
Information

Please see Important Safety Information:

- Hypersensitivity reactions manifested by symptoms, including, but not limited to anaphylaxis, dyspnea, flushing, and chest pain have been observed with TORISEL.
- Serum glucose, serum cholesterol, and triglycerides should be tested before and during treatment with TORISEL.

The use of TORISEL is likely to result in hyperglycemia and hyperlipidemia. This may result in the need for

TORISEL®
(temsirolimus) injection



TORISEL®—The first and only IV mTOR inhibitor indicated for advanced RCC[†]

Change expectations with TORISEL

References

1. TORISEL® Kit (temsirolimus) Prescribing Information, Wyeth Pharmaceuticals Inc.
2. Hudes G, Carducci M, Tomczak P, et al. Temsirolimus, interferon alfa, or both for advanced renal-cell carcinoma. *N Engl J Med.* 2007;356:2271-2281.
3. Buxton ILO. Pharmacokinetics and pharmacodynamics: the dynamics of drug absorption, distribution, action, and elimination. In: Brunton LL, ed. *Goodman & Gilman's The Pharmacological Basis of Therapeutics*. 11th ed. New York, NY: McGraw-Hill; 2006:1-7.
4. Weingart SN, Brown E, Bach PB, et al. NCCN task force report: oral chemotherapy. *J Natl Compr Canc Netw.* 2008;6(suppl 3):S-1–S-14.

- Weekly IV administration provides monitoring opportunities
 - Enables physician monitoring of dose adherence[‡]
 - Enables weekly monitoring for possible adverse reactions

^{*}A comparison is considered statistically significant if the P-value is <0.0159 (O'Brien-Fleming boundary at 446 deaths).

[†]Based on Cox proportional hazard model stratified by prior nephrectomy and region.



© 2009, Wyeth Pharmaceuticals Inc., Philadelphia, PA 19101

September 2009

253629-01

Safety Info



Please see
Prescribing
Information



Please see Important Safety Information:

- Hypersensitivity reactions manifested by symptoms, including, but not limited to anaphylaxis, dyspnea, flushing, and chest pain have been observed with TORISEL.
- Serum glucose, serum cholesterol, and triglycerides should be tested before and during treatment with TORISEL.

The use of TORISEL is likely to result in hyperglycemia and hyperlipidemia. This may result in the need for



Cover



Survival and 2nd End Points



Tolerability and Safety



Predictability / Attributes of IV



NCCN Recommendation



Reimbursement Support



Study Design



Mechanism of Action



Summary



Discussions

HIGHLIGHTS OF PRESCRIBING INFORMATION

These highlights do not include all the information needed to use TORISEL® safely and effectively. See [full prescribing information](#) for TORISEL.

TORISEL Kit (temsirolimus) injection, for intravenous infusion only
Initial U.S. Approval: 2007

INDICATIONS AND USAGE

TORISEL® is a kinase inhibitor indicated for the treatment of advanced renal cell carcinoma. (1)

DOSAGE AND ADMINISTRATION

- The recommended dose of TORISEL is 25 mg infused over a 30-60 minute period once a week. Treat until disease progression or unacceptable toxicity. (2.1)
- Antihistamine pre-treatment is recommended. (2.2)
- TORISEL (temsirolimus) injection vial contents must first be diluted with the enclosed diluent before diluting the resultant solution with 250 mL of 0.9% sodium chloride injection. (2.5)

DOSAGE FORMS AND STRENGTHS

TORISEL injection, 25 mg/mL supplied with DILUENT for TORISEL. (3)

CONTRAINDICATIONS

- None. (4)

WARNINGS AND PRECAUTIONS

- To treat hypersensitivity reactions stop TORISEL and treat with an antihistamine. TORISEL may be restarted at physician discretion at a slower rate. (5.1)
- Hyperglycemia and hyperlipidemia are likely and may require treatment. Monitor glucose and lipid profiles. (5.2, 5.5)
- Infections may result from immunosuppression. (5.3)

FULL PRESCRIBING INFORMATION: CONTENTS*

1 INDICATIONS AND USAGE	6 ADVERSE REACTIONS
2 DOSAGE AND ADMINISTRATION	6.1 Clinical Trials Experience
2.1 Advanced Renal Cell Carcinoma	7 DRUG INTERACTIONS
2.2 Premedication	7.1 Agents Inducing CYP3A Metabolism

Change expectations

Cover

S

Survival and 2nd End Points

T

Tolerability and Safety

P

Predictability / Attributes of IV

NCCN

NCCN Recommendation

Support

Reimbursement Support

Study Design

Study Design

MOA

Mechanism of Action

Summary

Summary

- Monitor for symptoms or radiographic changes of interstitial lung disease (ILD). If ILD is suspected, discontinue TORISEL, and consider use of corticosteroids and/or antibiotics. (5.4)
- Bowel perforation may occur. Evaluate fever, abdominal pain, bloody stools, and/or acute abdomen promptly. (5.6)
- Renal failure, sometimes fatal, has occurred. Monitor renal function at baseline and while on TORISEL. (5.7)
- Due to abnormal wound healing, use TORISEL with caution in the perioperative period. (5.8)
- Live vaccinations and close contact with those who received live vaccines should be avoided. (5.12)
- Women of childbearing potential should be advised of the potential hazard to the fetus and to avoid becoming pregnant. (5.13)

ADVERSE REACTIONS

The most common adverse reactions (incidence $\geq 30\%$) are rash, asthenia, mucositis, nausea, edema, and anorexia. The most common laboratory abnormalities (incidence $\geq 30\%$) are anemia, hyperglycemia, hyperlipidemia, hypertriglyceridemia, elevated alkaline phosphatase, elevated serum creatinine, lymphopenia, hypophosphatemia, thrombocytopenia, elevated AST, and leukopenia. (6)

To report SUSPECTED ADVERSE REACTIONS, contact Wyeth Pharmaceuticals Inc. at 1-800-934-5556 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch

DRUG INTERACTIONS

Strong inducers of CYP3A4/5 and inhibitors of CYP3A4 may affect concentrations of the primary metabolite of TORISEL. If alternatives cannot be used, dose modifications of TORISEL are recommended. (7.1, 7.2)

See 17 for PATIENT COUNSELING INFORMATION

Revised: 09/2008



Discussions

live vaccines, while on TORISEL should be avoided. [see *Warnings and Precautions (5.12)*].

• Pregnancy

TORISEL can cause fetal harm. Women of childbearing potential should be advised to avoid becoming pregnant throughout treatment and for 3 months after TORISEL therapy has stopped. Men with partners of childbearing potential should use reliable contraception throughout treatment and are recommended to continue this for 3 months after the last dose of TORISEL. [see *Warnings and Precautions (5.13)*].

Wyeth®

Wyeth Pharmaceuticals Inc.
Philadelphia, PA 19101

Manufactured for: Wyeth Pharmaceuticals Inc. Philadelphia, PA 19101

TORISEL® (temsirolimus) injection is manufactured by: Pierre Fabre Medicament Production, Aquitaine Pharm International, Avenue du Bearn, F64320 Idron, France

DILUENT for TORISEL® is manufactured by: Ben Venue Laboratories, Inc., Bedford, Ohio
44146-0568

W10524C004
ET01
Rev 09/08

20

Change expectations

S

T

P

NCCN

Support

Study Design

MOA

Summary

Cover

Survival and 2nd End Points

Tolerability and Safety

Predictability / Attributes of IV

NCCN Recommendation

Reimbursement Support

Study Design

Mechanism of Action

Summary

Discussions



DRUG INTERACTIONS WITH CYP3A INDUCERS AND INHIBITORS FOR TORISEL® (temsirolimus) injection

Cytochrome P450 3A4 (CYP3A4) is the major isozyme responsible for the formation of 5 temsirolimus metabolites.¹ Sirolimus, an active metabolite of temsirolimus, is the principal metabolite in humans following intravenous treatment and is also known to be metabolized by the CYP3A4 isoenzymes.¹ The following tables are not all-inclusive. Care should be exercised when drugs or other substances that affect CYP3A4 are administered concomitantly with temsirolimus.¹

CYP3A4/5 Inducers

Strong inducers of CYP3A4/5 may decrease exposure of the active metabolite, sirolimus. **Therefore, concomitant treatment with agents that have strong CYP3A4/5 induction potential should be avoided.** If alternative treatment cannot be administered, a **TORISEL dose increase up to 50 mg per week should be considered.**¹

Examples of CYP3A Inducers¹

Generic	Brand Name
Anticonvulsants	
carbamazepine	Tegretol®
phenobarbital	N/A
phenytoin	Dilantin®
Antibiotics	
rifampin/rifampicin	Rifadin®
rifabutin	Mycobutin®



- TORISEL must be stored under refrigeration at 2°C to 8°C (36°F to 46°F) and protected from light¹
- TORISEL must be diluted twice before administration¹

Please see inside for Important Safety Information.



Please see accompanying full Prescribing Information.

Reference: 1. TORISEL™ Kit (temsirolimus) Prescribing Information, Wyeth Pharmaceuticals Inc.

Wyeth®

© 2008, Wyeth Pharmaceuticals Inc., Philadelphia, PA 19101

January 2008

216203-01



Cover



Survival and 2°
End Points



Tolerability and
Safety



Predictability /
Attributes of IV



NCCN
Recommendation



Reimbursement
Support



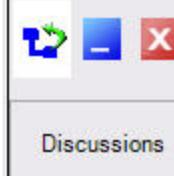
Study Design



Mechanism of
Action



Summary





ORIGINAL ARTICLE

Temsirolimus, Interferon Alfa, or Both for Advanced Renal-Cell Carcinoma

Gary Hudes, M.D., Michael Carducci, M.D., Piotr Tomiczak, M.D.,
 Janice Dutcher, M.D., Robert Figlin, M.D., Anil Kapoor, M.D.,
 Elzbieta Staroslawska, M.D., Jeffrey Sosman, M.D., David McDermott, M.D.,
 István Bodrogi, M.D., Zoran Kovacevic, M.D., Vladimir Lesovoy, M.D.,
 Ingo G.H. Schmidt-Wolf, M.D., Olga Barbarash, M.D., Erhan Gokmen, M.D.,
 Timothy O'Toole, M.S., Stephanie Lustgarten, M.S.,
 Laurence Moore, M.D., Ph.D., and Robert J. Motzer, M.D.,
 for the Global ARCC Trial*

ABSTRACT

BACKGROUND

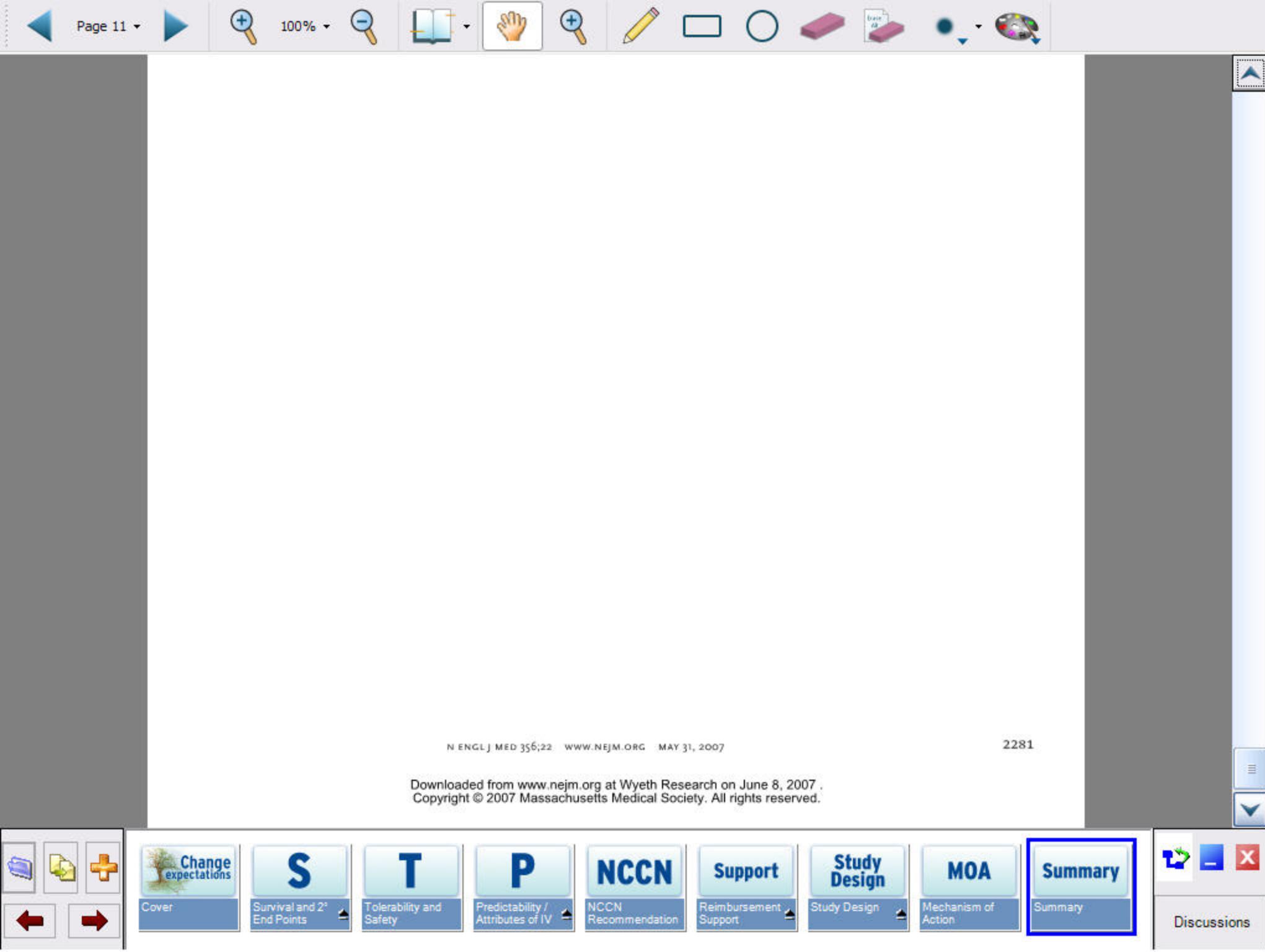
Interferon alfa is widely used for metastatic renal-cell carcinoma but has limited efficacy and tolerability. Temsirolimus, a specific inhibitor of the mammalian target of rapamycin kinase, may benefit patients with this disease.

METHODS

In this multicenter, phase 3 trial, we randomly assigned 626 patients with previously untreated, poor-prognosis metastatic renal-cell carcinoma to receive 25 mg of intravenous temsirolimus weekly, 3 million U of interferon alfa (with an increase to 18 million U) subcutaneously three times weekly, or combination therapy with 15 mg of temsirolimus weekly plus 6 million U of interferon alfa three times weekly. The primary end point was overall survival in comparisons of the temsirolimus group and the combination-therapy group with the interferon group.

From the Fox Chase Cancer Center, Philadelphia (G.H.); Sidney Kimmel Comprehensive Cancer Center, Baltimore (M.C.); Klinika Onkologii, Oddzial Chemicoterapii, Poznań, Poland (P.T.); Our Lady of Mercy Medical Center, Bronx, NY (J.D.); University of California, Los Angeles, Los Angeles (R.F.); McMaster University, Hamilton, ON, Canada (A.K.); Lublin Oncological Center, Lublin, Poland (E.S.); Vanderbilt University Medical Center, Nashville (J.S.); Beth Israel Deaconess Medical Center, Boston (D.M.); National Institute of Oncology, Budapest, Hungary (I.B.); Military Medical Academy, Belgrade, Serbia (Z.K.); Regional Clinical Center of Urology and Ne-





N ENGL J MED 356;22 WWW.NEJM.ORG MAY 31, 2007

2281

Downloaded from www.nejm.org at Wyeth Research on June 8, 2007.
Copyright © 2007 Massachusetts Medical Society. All rights reserved.



Discussions



Product-Specific J Code for TORISEL® (temsirolimus) injection

J9330 — Injection, temsirolimus

1 mg = 1 Billable Unit

Temsirolimus injection (TORISEL) has a product-specific J code: J9330. Please note that J9330 represents 1 mg. This code should be used in the appropriate field of the CMS 1500 form when administering temsirolimus in an office-based setting, along with other pertinent information, as follows¹:

		1500			
18. RESERVED FOR LOCAL USE				CARRIER	
21. DIAGNOSIS OR NATURE OF ILLNESS OR INJURY (Relate items 1, 2, 3 or 4 to Item 24E by Line)				PATIENT AND INSURED INFORMATION	
1. L _____	3. L _____	<input type="checkbox"/> 1. TUMOR(S) PRIMARY SITE, PRINCIPAL <input type="checkbox"/> 2. TUMOR(S) SECONDARY SITE, PRINCIPAL <input type="checkbox"/> 3. TUMOR(S) SECONDARY SITE, ASSISTANT <input type="checkbox"/> 4. TUMOR(S) ASSISTANT SITE		<input type="checkbox"/> 1. TUMOR(S) PRIMARY SITE, ASSISTANT <input type="checkbox"/> 2. TUMOR(S) SECONDARY SITE, ASSISTANT <input type="checkbox"/> 3. TUMOR(S) ASSISTANT SITE, ASSISTANT	
2. L _____	4. L _____	<input type="checkbox"/> 5. AUTOIMMUNE DISEASE <input type="checkbox"/> 6. AUTOINFLAMMATION <input type="checkbox"/> 7. AUTOINFLAMMATION, ASSISTANT		<input type="checkbox"/> 8. AUTOIMMUNE DISEASE, ASSISTANT <input type="checkbox"/> 9. AUTOINFLAMMATION <input type="checkbox"/> 10. AUTOINFLAMMATION, ASSISTANT	
<input type="checkbox"/> 11. ANEMIA <input type="checkbox"/> 12. ASTHMA <input type="checkbox"/> 13. CEREBROVASCULAR DISEASE <input type="checkbox"/> 14. CHRONIC OBSTRUCTIVE PULMONARY DISEASE <input type="checkbox"/> 15. DIABETES MELLITUS <input type="checkbox"/> 16. EPILEPSY <input type="checkbox"/> 17. HYPERTENSION <input type="checkbox"/> 18. HYPERLIPIDEMIA <input type="checkbox"/> 19. INFECTION <input type="checkbox"/> 20. ISCHEMIC HEART DISEASE <input type="checkbox"/> 21. METABOLIC DISORDERS <input type="checkbox"/> 22. NEUROLOGIC DISEASE <input type="checkbox"/> 23. OBSTETRIC <input type="checkbox"/> 24. OSTEOPOROSIS <input type="checkbox"/> 25. PULMONARY DISEASE <input type="checkbox"/> 26. RHEUMATIC DISEASE <input type="checkbox"/> 27. STROKE <input type="checkbox"/> 28. VASCULAR DISEASE				<input type="checkbox"/> 11. ANEMIA <input type="checkbox"/> 12. ASTHMA <input type="checkbox"/> 13. CEREBROVASCULAR DISEASE <input type="checkbox"/> 14. CHRONIC OBSTRUCTIVE PULMONARY DISEASE <input type="checkbox"/> 15. DIABETES MELLITUS <input type="checkbox"/> 16. EPILEPSY <input type="checkbox"/> 17. HYPERTENSION <input type="checkbox"/> 18. HYPERLIPIDEMIA <input type="checkbox"/> 19. INFECTION <input type="checkbox"/> 20. ISCHEMIC HEART DISEASE <input type="checkbox"/> 21. METABOLIC DISORDERS <input type="checkbox"/> 22. NEUROLOGIC DISEASE <input type="checkbox"/> 23. OBSTETRIC <input type="checkbox"/> 24. OSTEOPOROSIS <input type="checkbox"/> 25. PULMONARY DISEASE <input type="checkbox"/> 26. RHEUMATIC DISEASE <input type="checkbox"/> 27. STROKE <input type="checkbox"/> 28. VASCULAR DISEASE	
<input type="checkbox"/> 29. ANEMIA <input type="checkbox"/> 30. ASTHMA <input type="checkbox"/> 31. CEREBROVASCULAR DISEASE <input type="checkbox"/> 32. CHRONIC OBSTRUCTIVE PULMONARY DISEASE <input type="checkbox"/> 33. DIABETES MELLITUS <input type="checkbox"/> 34. EPILEPSY <input type="checkbox"/> 35. HYPERTENSION <input type="checkbox"/> 36. HYPERLIPIDEMIA <input type="checkbox"/> 37. INFECTION <input type="checkbox"/> 38. ISCHEMIC HEART DISEASE <input type="checkbox"/> 39. METABOLIC DISORDERS <input type="checkbox"/> 40. NEUROLOGIC DISEASE <input type="checkbox"/> 41. OBSTETRIC <input type="checkbox"/> 42. OSTEOPOROSIS <input type="checkbox"/> 43. PULMONARY DISEASE <input type="checkbox"/> 44. RHEUMATIC DISEASE <input type="checkbox"/> 45. STROKE <input type="checkbox"/> 46. VASCULAR DISEASE				<input type="checkbox"/> 29. ANEMIA <input type="checkbox"/> 30. ASTHMA <input type="checkbox"/> 31. CEREBROVASCULAR DISEASE <input type="checkbox"/> 32. CHRONIC OBSTRUCTIVE PULMONARY DISEASE <input type="checkbox"/> 33. DIABETES MELLITUS <input type="checkbox"/> 34. EPILEPSY <input type="checkbox"/> 35. HYPERTENSION <input type="checkbox"/> 36. HYPERLIPIDEMIA <input type="checkbox"/> 37. INFECTION <input type="checkbox"/> 38. ISCHEMIC HEART DISEASE <input type="checkbox"/> 39. METABOLIC DISORDERS <input type="checkbox"/> 40. NEUROLOGIC DISEASE <input type="checkbox"/> 41. OBSTETRIC <input type="checkbox"/> 42. OSTEOPOROSIS <input type="checkbox"/> 43. PULMONARY DISEASE <input type="checkbox"/> 44. RHEUMATIC DISEASE <input type="checkbox"/> 45. STROKE <input type="checkbox"/> 46. VASCULAR DISEASE	
<input type="checkbox"/> 47. ANEMIA <input type="checkbox"/> 48. ASTHMA <input type="checkbox"/> 49. CEREBROVASCULAR DISEASE <input type="checkbox"/> 50. CHRONIC OBSTRUCTIVE PULMONARY DISEASE <input type="checkbox"/> 51. DIABETES MELLITUS <input type="checkbox"/> 52. EPILEPSY <input type="checkbox"/> 53. HYPERTENSION <input type="checkbox"/> 54. HYPERLIPIDEMIA <input type="checkbox"/> 55. INFECTION <input type="checkbox"/> 56. ISCHEMIC HEART DISEASE <input type="checkbox"/> 57. METABOLIC DISORDERS <input type="checkbox"/> 58. NEUROLOGIC DISEASE <input type="checkbox"/> 59. OBSTETRIC <input type="checkbox"/> 60. OSTEOPOROSIS <input type="checkbox"/> 61. PULMONARY DISEASE <input type="checkbox"/> 62. RHEUMATIC DISEASE <input type="checkbox"/> 63. STROKE <input type="checkbox"/> 64. VASCULAR DISEASE				<input type="checkbox"/> 47. ANEMIA <input type="checkbox"/> 48. ASTHMA <input type="checkbox"/> 49. CEREBROVASCULAR DISEASE <input type="checkbox"/> 50. CHRONIC OBSTRUCTIVE PULMONARY DISEASE <input type="checkbox"/> 51. DIABETES MELLITUS <input type="checkbox"/> 52. EPILEPSY <input type="checkbox"/> 53. HYPERTENSION <input type="checkbox"/> 54. HYPERLIPIDEMIA <input type="checkbox"/> 55. INFECTION <input type="checkbox"/> 56. ISCHEMIC HEART DISEASE <input type="checkbox"/> 57. METABOLIC DISORDERS <input type="checkbox"/> 58. NEUROLOGIC DISEASE <input type="checkbox"/> 59. OBSTETRIC <input type="checkbox"/> 60. OSTEOPOROSIS <input type="checkbox"/> 61. PULMONARY DISEASE <input type="checkbox"/> 62. RHEUMATIC DISEASE <input type="checkbox"/> 63. STROKE <input type="checkbox"/> 64. VASCULAR DISEASE	
<input type="checkbox"/> 65. ANEMIA <input type="checkbox"/> 66. ASTHMA <input type="checkbox"/> 67. CEREBROVASCULAR DISEASE <input type="checkbox"/> 68. CHRONIC OBSTRUCTIVE PULMONARY DISEASE <input type="checkbox"/> 69. DIABETES MELLITUS <input type="checkbox"/> 70. EPILEPSY <input type="checkbox"/> 71. HYPERTENSION <input type="checkbox"/> 72. HYPERLIPIDEMIA <input type="checkbox"/> 73. INFECTION <input type="checkbox"/> 74. ISCHEMIC HEART DISEASE <input type="checkbox"/> 75. METABOLIC DISORDERS <input type="checkbox"/> 76. NEUROLOGIC DISEASE <input type="checkbox"/> 77. OBSTETRIC <input type="checkbox"/> 78. OSTEOPOROSIS <input type="checkbox"/> 79. PULMONARY DISEASE <input type="checkbox"/> 80. RHEUMATIC DISEASE <input type="checkbox"/> 81. STROKE <input type="checkbox"/> 82. VASCULAR DISEASE				<input type="checkbox"/> 65. ANEMIA <input type="checkbox"/> 66. ASTHMA <input type="checkbox"/> 67. CEREBROVASCULAR DISEASE <input type="checkbox"/> 68. CHRONIC OBSTRUCTIVE PULMONARY DISEASE <input type="checkbox"/> 69. DIABETES MELLITUS <input type="checkbox"/> 70. EPILEPSY <input type="checkbox"/> 71. HYPERTENSION <input type="checkbox"/> 72. HYPERLIPIDEMIA <input type="checkbox"/> 73. INFECTION <input type="checkbox"/> 74. ISCHEMIC HEART DISEASE <input type="checkbox"/> 75. METABOLIC DISORDERS <input type="checkbox"/> 76. NEUROLOGIC DISEASE <input type="checkbox"/> 77. OBSTETRIC <input type="checkbox"/> 78. OSTEOPOROSIS <input type="checkbox"/> 79. PULMONARY DISEASE <input type="checkbox"/> 80. RHEUMATIC DISEASE <input type="checkbox"/> 81. STROKE <input type="checkbox"/> 82. VASCULAR DISEASE	
<input type="checkbox"/> 83. ANEMIA <input type="checkbox"/> 84. ASTHMA <input type="checkbox"/> 85. CEREBROVASCULAR DISEASE <input type="checkbox"/> 86. CHRONIC OBSTRUCTIVE PULMONARY DISEASE <input type="checkbox"/> 87. DIABETES MELLITUS <input type="checkbox"/> 88. EPILEPSY <input type="checkbox"/> 89. HYPERTENSION <input type="checkbox"/> 90. HYPERLIPIDEMIA <input type="checkbox"/> 91. INFECTION <input type="checkbox"/> 92. ISCHEMIC HEART DISEASE <input type="checkbox"/> 93. METABOLIC DISORDERS <input type="checkbox"/> 94. NEUROLOGIC DISEASE <input type="checkbox"/> 95. OBSTETRIC <input type="checkbox"/> 96. OSTEOPOROSIS <input type="checkbox"/> 97. PULMONARY DISEASE <input type="checkbox"/> 98. RHEUMATIC DISEASE <input type="checkbox"/> 99. STROKE <input type="checkbox"/> 100. VASCULAR DISEASE				<input type="checkbox"/> 83. ANEMIA <input type="checkbox"/> 84. ASTHMA <input type="checkbox"/> 85. CEREBROVASCULAR DISEASE <input type="checkbox"/> 86. CHRONIC OBSTRUCTIVE PULMONARY DISEASE <input type="checkbox"/> 87. DIABETES MELLITUS <input type="checkbox"/> 88. EPILEPSY <input type="checkbox"/> 89. HYPERTENSION <input type="checkbox"/> 90. HYPERLIPIDEMIA <input type="checkbox"/> 91. INFECTION <input type="checkbox"/> 92. ISCHEMIC HEART DISEASE <input type="checkbox"/> 93. METABOLIC DISORDERS <input type="checkbox"/> 94. NEUROLOGIC DISEASE <input type="checkbox"/> 95. OBSTETRIC <input type="checkbox"/> 96. OSTEOPOROSIS <input type="checkbox"/> 97. PULMONARY DISEASE <input type="checkbox"/> 98. RHEUMATIC DISEASE <input type="checkbox"/> 99. STROKE <input type="checkbox"/> 100. VASCULAR DISEASE	

- Field 19 – Description:** Identify product as either temsirolimus injection or TORISEL; dose method of administration as IV infusion; and 11-digit NDC code as 00008-1179-01, TORISEL Kit injection, 25 mg/mL.²
- Field 21 – Diagnosis Code:** Use the ICD-9-CM codes 189.0-189.1.³



Cover

Survival and 2nd End Points

Tolerability and Safety



Predictability / Attributes of IV



NCCN Recommendation



Reimbursement Support



Study Design



Mechanism of Action



Summary



Discussions



*CPT® is a registered trademark of the American Medical Association.

- References:**
1. Centers for Medicare & Medicaid Services. 2009 Table of Drugs. <http://www.cms.hhs.gov/HCPCSReleaseCodeSets/ANHCPCS/itemdetail.asp?filterType=none&filterByDID=-99&sortByDID=1&sortOrder=descending&itemID=CMS12I6705&intNumPerPage=10>. Accessed November 3, 2008.
 2. TORISEL® Kit (temsirolimus) Prescribing Information, Wyeth Pharmaceuticals Inc.
 3. US Centers for Disease Control and Prevention – National Center for Health Statistics. 2007 ICD-9-CM rich text files. ftp://ftp.cdc.gov/pub/Health_Statistics/NCHS/Publications/ICD9-CM/2007/. Accessed July 16, 2008.

Wyeth®

© 2008, Wyeth Pharmaceuticals Inc., Philadelphia, PA 19101

November 2008

240218-01



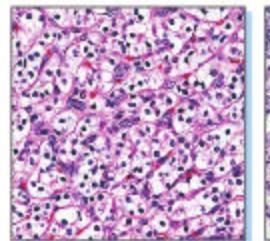


Advanced Renal Cell Carcinoma (RCC): Not a Single Disease

Important Variations Between Different Types of RCC¹

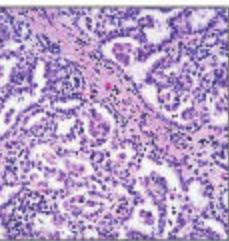
- Histologies
- Genetic causes

5 Different Histologies of RCC and Their Incidence¹



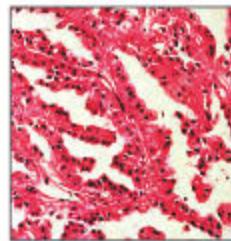
Clear cell

75%



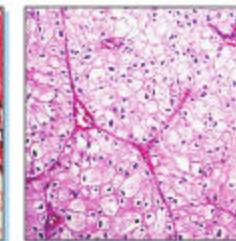
Papillary type 1

5%



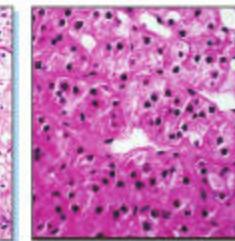
Papillary type 2

10%



Chromophobe

5%



Oncocytoma

5%

Gene* VHL

Met

FH

BHD

*von Hippel-Lindau (VHL) is a hereditary form of clear cell renal carcinoma. Hereditary papillary renal

KPS=Karnofsky performance status.
IFN- α =interferon-alpha.

Impact of the Number of MSKCC Risk Factors on Patient Outcomes^{2†}

No. of Risk Factors	Risk Groups	Median OS
3 or more	Poor	4.9 months
1 or 2	Intermediate	13.8 months
0	Favorable	29.6 months

OS=overall survival.

- >2 years difference in median OS between poor and favorable patients²
- Significant differences in OS across the 3 risk groups ($P<0.0001$)²

*ECOG PS to KPS: Proposed Conversion Table⁴

ECOG PS Score	KPS Score
0,1	100–80
2	70–60
3,4	50–10

ECOG PS=Eastern Cooperative Oncology Group Performance Status Scale.

[†]Retrospective analysis of 463 patients with advanced RCC receiving IFN- α as first-line systemic therapy in 6 prospective clinical trials.²

References: 1. Linehan WM, Walther MM, Zbar B. The genetic basis of cancer of the kidney. *J Urol.* 2003;170:2163-2172. 2. Motzer RJ, Bacik J, Murphy BA, et al. Interferon-alpha as a comparative treatment for clinical trials of new therapies against advanced renal cell carcinoma. *J Clin Oncol.* 2002;20:289-296. 3. Motzer RJ, Bacik J, Schwartz LH, et al. Prognostic factors for survival in previously treated patients with metastatic renal cell carcinoma. *J Clin Oncol.* 2004;22:454-463. 4. Buccheri G, Ferrigno D, Tamburini M. Karnofsky and ECOG performance status scoring in lung cancer: a prospective, longitudinal study of 536 patients from a single institution. *Eur J Cancer.* 1996;32A:1135-1141.

Wyeth®

© 2008, Wyeth Pharmaceuticals Inc., Philadelphia, PA 19101

January 2008

216116-01



Cover



Survival and 2°
End Points



Tolerability and
Safety



Predictability /
Attributes of IV



NCCN
Recommendation



Reimbursement
Support



Study Design



Mechanism of
Action



Summary



Discussions