ADCETRIS VISUAL AID REVIEW: sALCL

INTRODUCTION

Welcome to the ADCETRIS Visual Aid for Systemic Anaplastic Large Cell Lymphoma (sALCL) training module

This module, which is aligned to the visual aid, will explore the key elements of the visual aid as well as the core messaging of ADCETRIS with supporting evidence from pivotal trials.

LEARNING OBJECTIVES

By the end of this module, you should:

- Gain a thorough understanding of all information contained within the Visual Aid
- Be able to reference the proof source for information contained within the Visual Aid
- Use the visual aid to support a clear and concise sales presentation

THE VISUAL AID

The visual aid is a marketing tool used to support your presentation on the product information and the core messaging.

It highlights information on product efficacy with the data from clinical trials, lists approved indications, and discusses tolerability and safety along with the dosing and administration.

THERAPEUTIC INDICATIONS

ADCETRIS is indicated for:

- Relapsed or Refractory Systemic anaplastic large cell lymphoma (sALCL)
- Relapsed or Refractory Hodgkins Lymphoma (HL)
    - following autologous stem cell transplant (ASCT)

      or
    - following at least two prior therapies when ASCT or multi-agent chemotherapy is not a treatment option

Note: approved indication may vary in your local market

ADCETRIS VISUAL AIDS

Therefore, ADCETRIS has 2 visual aids, each relevant to the associated indication and contains the specific messaging for each patient type.

This module will focus on the patient with Relapsed/refractory systemic Anaplastic Large Cell Lymphoma (sALCL) and the core messages that help to define ADCETRIS in patient with sALCL.

ADCETRIS VISUAL AID OVERVIEW

To provide a high-level overview of the visual aid, let's review the various sections:

- Page 2 provides the approved therapeutic indications.
- Page 3 highlights the mechanism of action.
- Page 4 outlines the typical therapeutic pathway
- Page 5 explains the prognosis of patients with relapsed or refractory sALCL
- Page 6-13 discuss the pivotal clinical trial and its results
- Page 14 explains the dosing schedule
- Page 15 examines the number of cycles of ADCETRIS received by best response
- Page 16 lists the references
- Page 17-19 are reserved for addition of the local PI
- Page 20 summarizes information about efficacy, safety and dosing of ADCETRIS

INDICATIONS AND MECHANISM OF ACTION

Let's review each page in detail so you gain a comfort level navigating the visual aid.

The therapeutic indications are defined on page 2 and page 3 explains the mechanism of action of ADCETRIS.

As mentioned earlier, ADCETRIS is indicated in relapsed or refractory Systemic anaplastic large cell lymphoma (sALCL) and relapsed or refractory Hodgkin lymphoma (HL).

Note: approved indication may vary in your local market

ADCETRIS is a novel CD30-targeted antibody-drug conjugate that enables the potent cytotoxic drug monomethyl auristatin E (MMAE) to be delivered inside CD30+ cancer cells causing apoptosis disintegration of the cell and cell death).

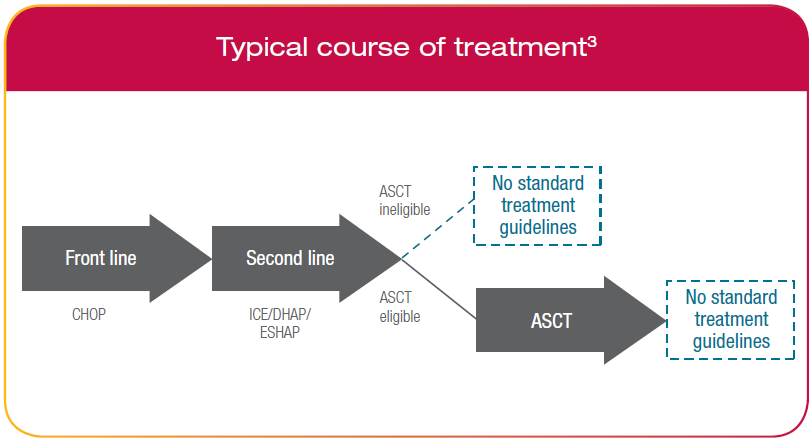
TREATMENT COURSE

The typical course of treatment is shown in this illustration. sALCL is an aggressive disease with no standard therapy in the relapsed or refractory setting.

Relapsed and refractory sALCL patients have a poor prognosis.

Up to 30% of patients do not respond to front line treatment and approximately 40% to 50% of patients with ALCL relapse following initial therapy. In addition, over 50% of patients who receive ASCT relapse within 10 years.

There have been no treatment advances for such patients with relapsed or refractory sALCL for over 30 years.



CHOP = cyclophosphamide, hydroxydaunorubicin, oncovin, prednisone.
ICE = ifosfamide, carboplatin, etoposide.
DHAP = dexamethasone, high-dose cytarabine, cisplatin.
ESHAP = etoposide, methylprednisolone, cytarabine, cisplatin.
National Comprehensive Cancer Network. NCCN Guidelines. Non-Hodgkin Lymphoma v3. 2012.3

PROGNOSIS FOR ALK- PATIENTS

The prognosis is significantly poorer for patients with Anaplastic lymphoma kinase negative (ALK-) sALCL compared to those with Anaplastic lymphoma kinase positive (ALK+) disease.

The 5-year overall survival and 5-year failure-free progression are significantly lower in the ALK- patients.

STUDY DESIGN

ADCETRIS was studied in an open-label, single arm, multicenter trial in which the single agent ADCETRIS was administered at 1.8 mg/kg intravenously over 30 minutes every 3 weeks in 58 heavily pre-treated patients with relapsed or refractory sALCL.

A maximum of 16 cycles of ADCETRIS were administered during the study and the patients were followed up every 12 weeks therafter.

The primary endpoint measured was the objective response rate (ORR) and the secondary endpoints were duration of response, complete remission, progression-free survival overall survival and adverse events' incidence and severity

PROGNOSIS AT BASELINE

The patients included in the trial had a poor prognosis at baseline. 72% had ALK- disease and the study population was heavily pre-treated with a median of 2 prior chemotherapy regimens. Sixty two percent of the patients had primary refractory disease, defined as failure to achieve a CR with front line therapy or they had relapsed within 3 months of front line therapy.

EFFICACY OF ADCETRIS

An independent review facility performed efficacy assessments to evaluate the objective response rate and duration of response.The objective response rate (ORR) includes patients who achieve complete remission (CR) and those that achieve partial remission (PR).

The results! …

59% of patients achieved Complete Remission and the objective response rate was 86%. Also, the response rates in ALK- and ALK+ patients were comparable.

The median duration of response in patients with complete remission was 26.3 months.

OVERALL SURVIVAL AND PROGRESSION FREE SURVIVAL

With ADCETRIS, the median overall survival was not reached at 33.4 months and the estimated 3-year survival rate was 63%.

Patients that achieved complete remission had a 14.6 month median progression-free survival.

Also, the PFS with ADCETRIS was significantly longer when compared with the most recent prior therapy.

So why use ADCETRIS … because ADCETRIS offers significant efficacy.

ADVERSE EVENTS

Now that we have discussed the efficacy of ADCETRIS, let's review the safety and tolerability profile.

Peripheral neuropathy was observed in 57% of the patients and 28% had pre-existing peripheral neuropathy.

The median time to onset of peripheral neuropathy events was 15 weeks and the median time to improvement or resolution of peripheral neuropathy was 14.1 weeks.

In case of grade 2 or 3 peripheral neuropathy a delay in dosing or dose reduction to 1.2 mg/kg is recommended.

Resolution or improvement in some or all peripheral neuropathy events was seen in 88% of patients.

DOSING

ADCETRIS offers a convenient dosing schedule every 3 weeks which is similar to other regimens.

Given intravenously only, the recommended dose is 1.8 mg/kg.

Patients who achieve stable disease or better should receive a minimum of 8 cycles and up to a maximum of 16 cycles (approximately 1 year)

Treatment should be continued until disease progression or unacceptable toxicity.

The maximum recommended dose is 180 mg.

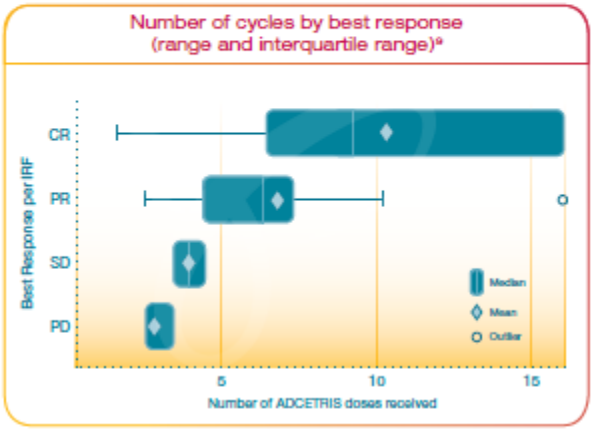
RESPONSE RATES AND NUMBER OF CYCLES

In reviewing the number of cycles of therapy in ALCL patients stratified by response category, it is notable that the patients who achieved either Complete Remission (CR) or Partial Remission (PR) received more cycles of therapy than patients with stable disease or progressive disease.

Overall, patients received a median of 7 cycles of ADCETRIS and those with objective response (OR) received a median of 8 cycles.

Remember, the dosing schedule recommends a minimum of 8 cycles and maximum of 16 cycles (approximately one year) unless the disease progresses or the patient experiences unacceptable toxicity.

Patients who achieved an objective response received more cycles of therapy[9]



Adapted from Pro et al. 2013

So it's important to discuss with your HCP that those patients who achieved an objective response in the trial received more cycles of therapy.

REFERENCES AND LOCAL PI

Page 16 includes a listing of the supporting references for the facts cited in the visual aid and pages 17-19 provide space for local prescribing information to be added.

SUMMARY

This page provides a summary of the key points for each of the core messages. Use it to close your presentation. Let's review:

ADCETRIS offers significant efficacy:

- Median overall survival has not been reached at 33.4 months (95% CI, 21.3 to not estimable)
- 86% of patients attain objective responses (ORR)
- 59% of patients achieve a complete remission (CR)
- 97 of patients experience tumor reduction
- Complete remission patients achieve a 14.6 month median PFS

ADCETRIS has a manageable adverse event profile

- Peripheral neuropathy is generally reversible and manageable through dose modification

ADCETRIS offers a convenient dosing schedule

- ADCETRIS offers 3 week dosing, similar to other regimens
- Patients who achieve stable disease or better should receive a minimum of 8 cycles and up to a maximum of 16 cycles (approximately 1 year)
    - Treatment should be continued until disease progression or unacceptable toxicity