Phase II Randomized, Multicenter Study of Lenalidomide vs Best Investigator's Choice in Relapsed/Refractory Mantle Cell Lymphoma: Results of the MCL-002 (SPRINT) Study

Abstract 626

**Trneny M, Lamy T, Walewski J, Jurczak W, Belada D,
Mayer J, Radford J, Alexeeva J, Osmanov D, Biyukov T, Patturajan M,
Casadebaig Bravo M-L, Arcaini L,
on behalf of SPRINT trial investigators**

prIME oncology

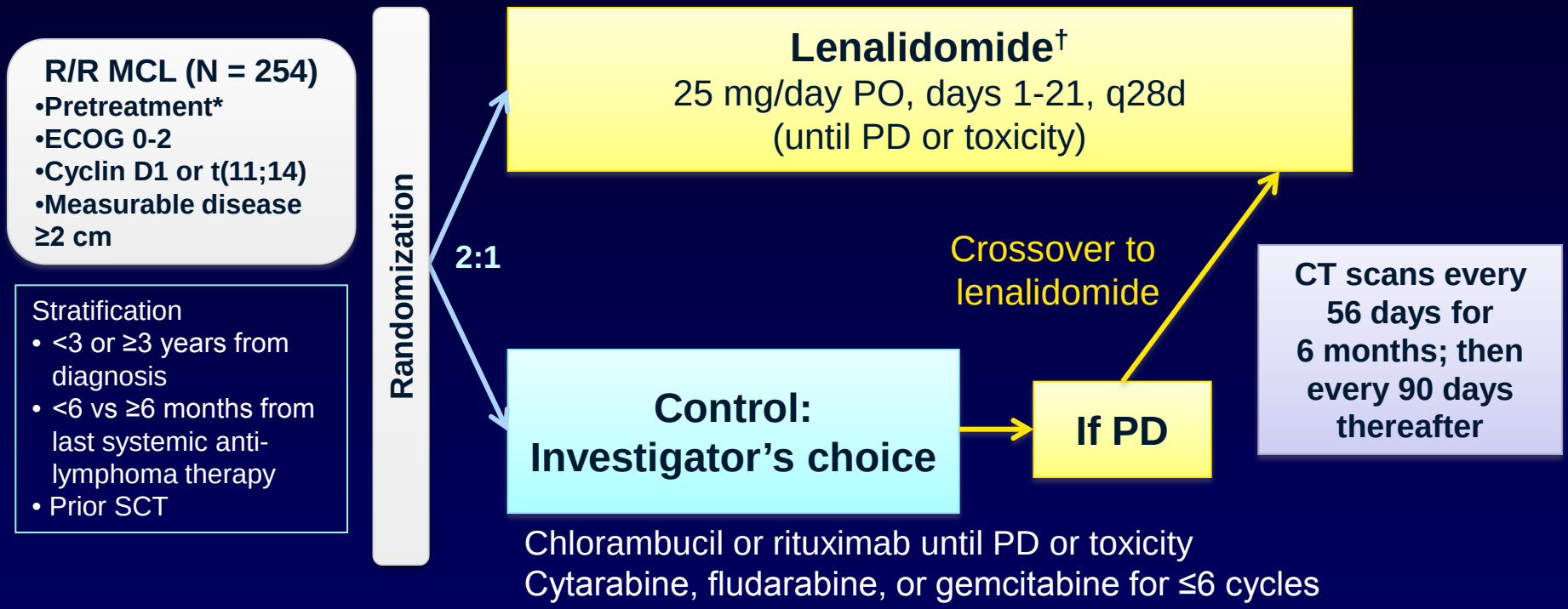
Background and Rationale

- **Mantle cell lymphoma (MCL) is an aggressive non-Hodgkin lymphoma with poor outcome, especially after failure of first-line treatment[1]**
- **Lenalidomide is an immunomodulatory drug with antineoplastic and antiproliferative effects[2-4]**
- **Lenalidomide has shown activity in multiple single-arm phase II studies (NHL-002, NHL-003, MCL-001) in patients with relapsed/refractory (R/R) MCL[5-7]**
- **First randomized trial with lenalidomide to compare with investigator's choice monotherapy in R/R MCL**

1. Goy A, et al. *Crit Rev Oncol Hematol*. 2011;80(1):69-86; 2. Qian Z, et al. *Leuk Res*. 2011;35(3):380-386; 3. Wu L, et al. *Clin Cancer Res*. 2008;14(14):4650-4657; 4. Zhang L, et al. *Am J Hematol.* 2009;84(9):553-559; 5. Habermann TM, et al. *Br J Haematol*. 2009;145(3):344-349; 6. Zinzani PL, et al. *Ann Oncol.* 2013;24(11):2892-2897; 7. Goy A, et al. *J Clin Oncol.* 2013;31(29):3688-3695.

Trneny M, et al. *Blood.* 2014;124: Abstract 626.

MCL-002 (SPRINT): Phase II European Multicenter, Open-Label Study (5/2009-3/2013)

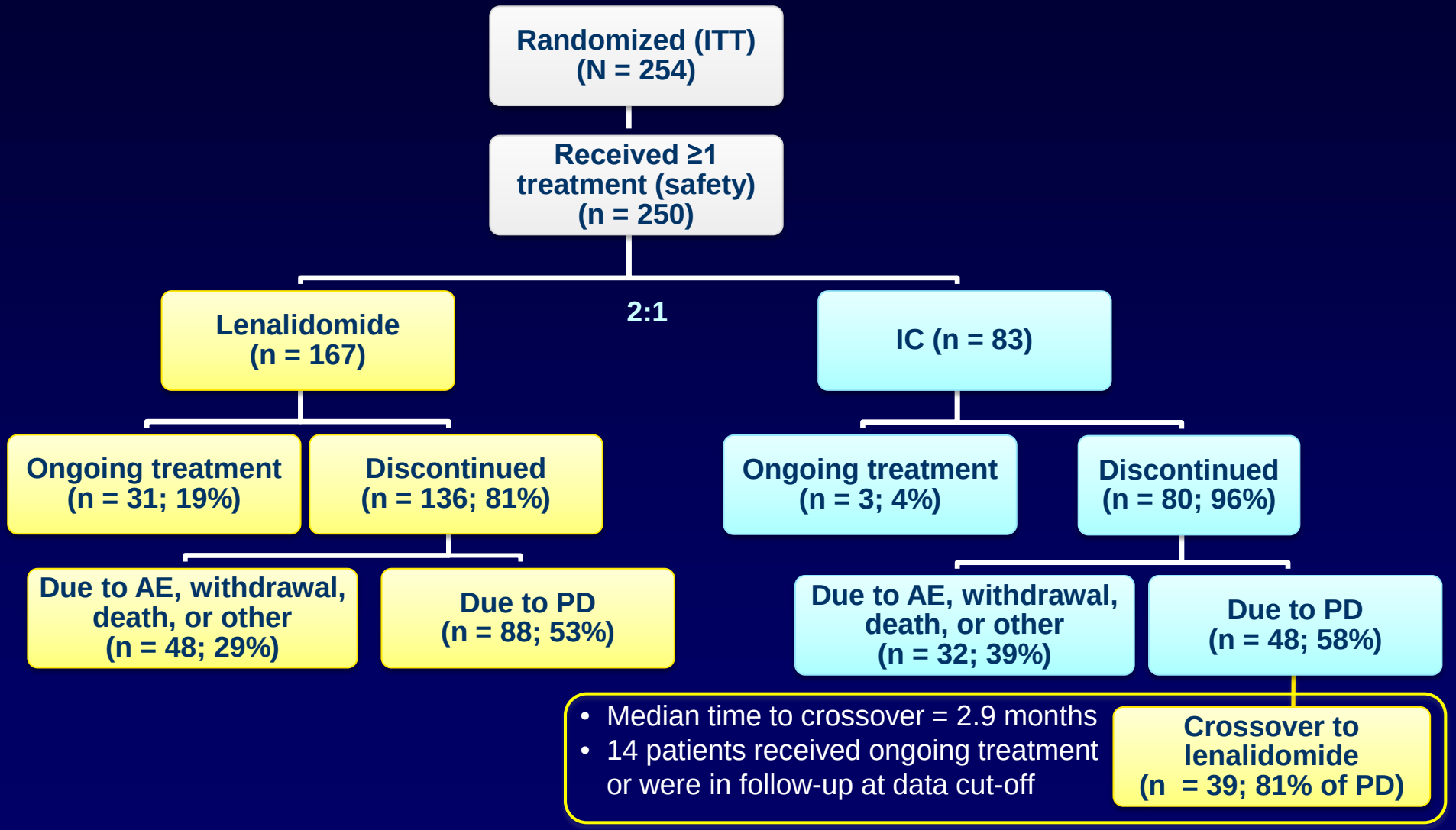


Primary endpoint: PFS (per independent central review)
Secondary endpoints: ORR, DOR, OS, and safety

NCT00875667; data cut-off March 7, 2014.
*Required ≥1 prior combination chemotherapy with alkylating agent, and anthracycline and/or cytarabine and/or fludarabine (± rituximab); ≤3 relapses or failure of prior therapy and ineligible for intensified treatment or SCT.
†Prophylaxis for all lenalidomide patients included aspirin or low molecular–weight heparin prophylaxis for thromboembolic events and allopurinol or equivalent with oral hydration during the first 7 days for tumor lysis syndrome.

Trneny M, et al. *Blood.* 2014;124: Abstract 626.

MCL-002: Disposition of Patients (5/2009-3/2013)



Trneny M, et al. *Blood.* 2014;124: Abstract 626.

Study Population

MCL-002: Baseline Demographics (ITT)

Characteristic, n (%)		Lenalidomide (n = 170)	IC (n = 84)
Median age, years (range)		68.5 (44-88)	68.5 (49-87)
Age ≥65 years		115 (68)	57 (68)
Male		123 (72)	63 (75)
ECOG PS*	0-1	142 (84)	73 (87)
≥2		27 (16)	11 (13)
≥3-year duration of MCL		76 (45)	39 (46)
MCL stage at diagnosis	I/II	13 (8)	3 (4)
III		30 (18)	20 (24)
IV		123 (72)	59 (70)
Missing		4 (2)	2 (2)
MIPI score	Low	42 (25)	21 (25)
Intermediate		66 (39)	37 (44)
High		**60 (35)**	**25 (30)**
Missing		2 (1)	1 (1)
High LDH (>ULN)†		**73 (43)**	**30 (36)**
High tumor burden‡		**81 (48)**	**28 (33)**
Bulky disease §		**37 (22)**	**13 (15)**
>30% Ki-67 index		**31 (18)**	**19 (23)**

- Despite stratification, patients receiving lenalidomide vs IC had a worse baseline prognostic profile (by ≥5%) due to higher disease risk by high-risk MIPI, high LDH, high tumor burden, and bulky disease

Trneny M, et al. *Blood.* 2014;124: Abstract 626.

MCL-002: Baseline Treatment History (ITT)

Characteristic, n (%)	Lenalidomide (n = 170)	IC (n = 84)
Median number of prior treatment regimens (range)	2 (1-5)	2 (1-4)
Number of prior systemic anti-lymphoma therapies		
1	**55 (32)**	**37 (44)**
2	70 (41)	23 (27)
3	36 (21)	20 (24)
≥4	9 (5)	4 (5)
Time from last prior systemic anti-lymphoma therapy		
<6 months	71 (42)	36 (43)
≥6 months	95 (56)	47 (56)
Best response to last prior systemic anti-lymphoma therapy		
CR/CRu	58 (34)	29 (35)
PR	42 (25)	30 (36)
SD	31 (18)	9 (11)
PD	33 (19)	10 (12)
Unknown	6 (4)	6 (7)
Received autologous SCT	30 (18)	18 (21)

37% Refractory (SD + PD: 31 (18) + 33 (19))

23% Refractory (SD + PD: 9 (11) + 10 (12))

Note: Baseline treatment history and prior response are missing for several patients in each arm.

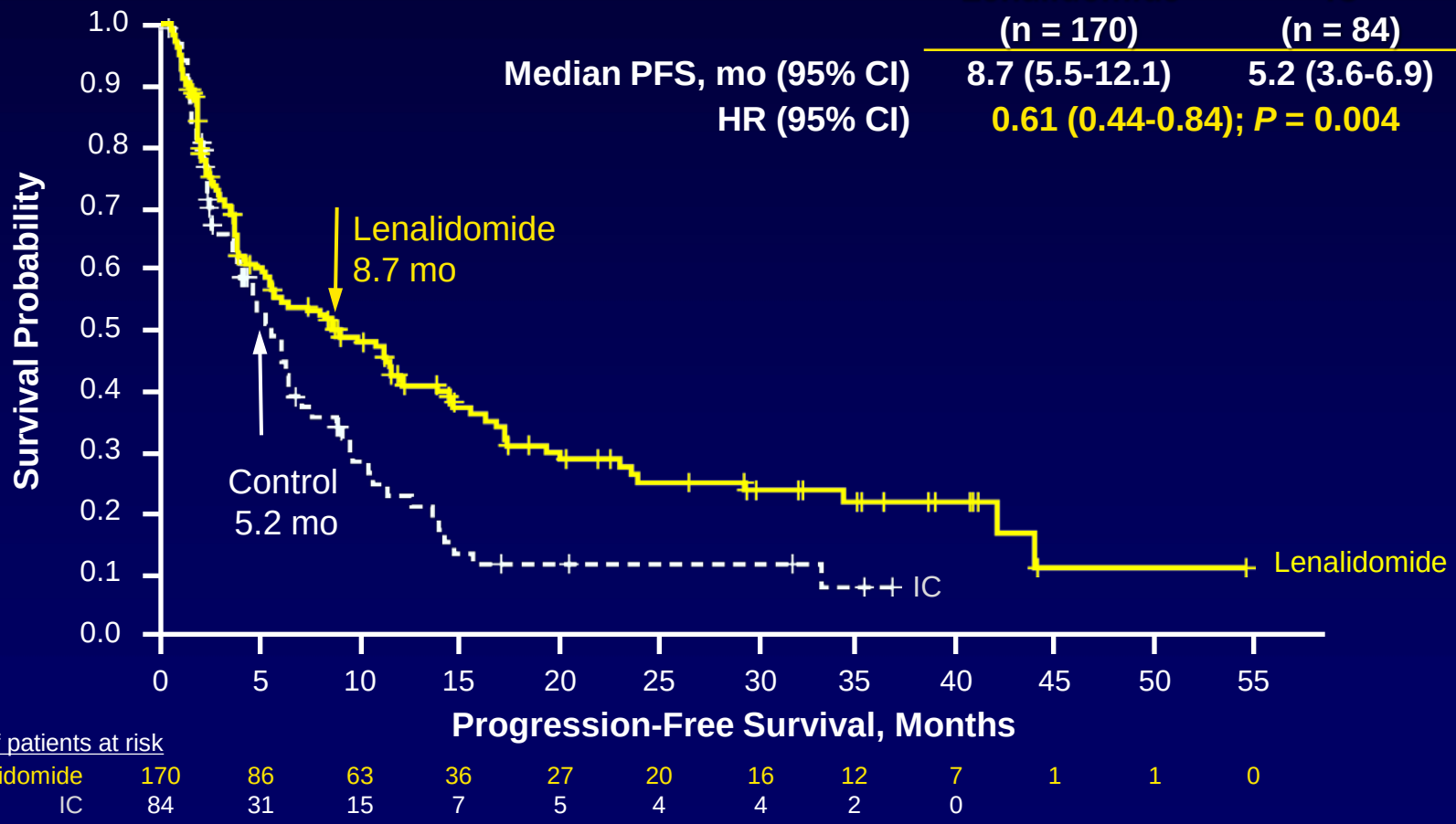
Trneny M, et al. *Blood.* 2014;124: Abstract 626.

Efficacy

MCL-002: Progression-Free Survival (ITT)*

Lenalidomide vs IC showed a 39% reduction in the risk of PD or death, reflected as an estimated improvement in median PFS of 3.5 months

	Lenalidomide (n = 170)	IC (n = 84)
Median PFS, mo (95% CI)	8.7 (5.5-12.1)	5.2 (3.6-6.9)
HR (95% CI)	0.61 (0.44-0.84); *P* = 0.004	



Number of patients at risk

Lenalidomide	170	86	63	36	27	20	16	12	7	1	1	0
IC	84	31	15	7	5	4	4	2	0			

Median follow-up time: 15.9 months

Trneny M, et al. *Blood.* 2014;124: Abstract 626.

*ICR, Data cut-off March 7, 2014.

MCL-002: Efficacy (ITT)*

Efficacy, n (%)†	Lenalidomide (n = 170)	IC (n = 84)	*P* value
ORR	**68 (40)**	**9 (11)**	**<.001**
CR/CRu	**8 (5)**	**0**	**.043**
PR	60 (35)	9 (11)	–
PD	34 (20)	26 (31)	–
Median DOR, months (95% CI)	16.0 (9.5-20.0)	10.4 (8.4-18.6)	–

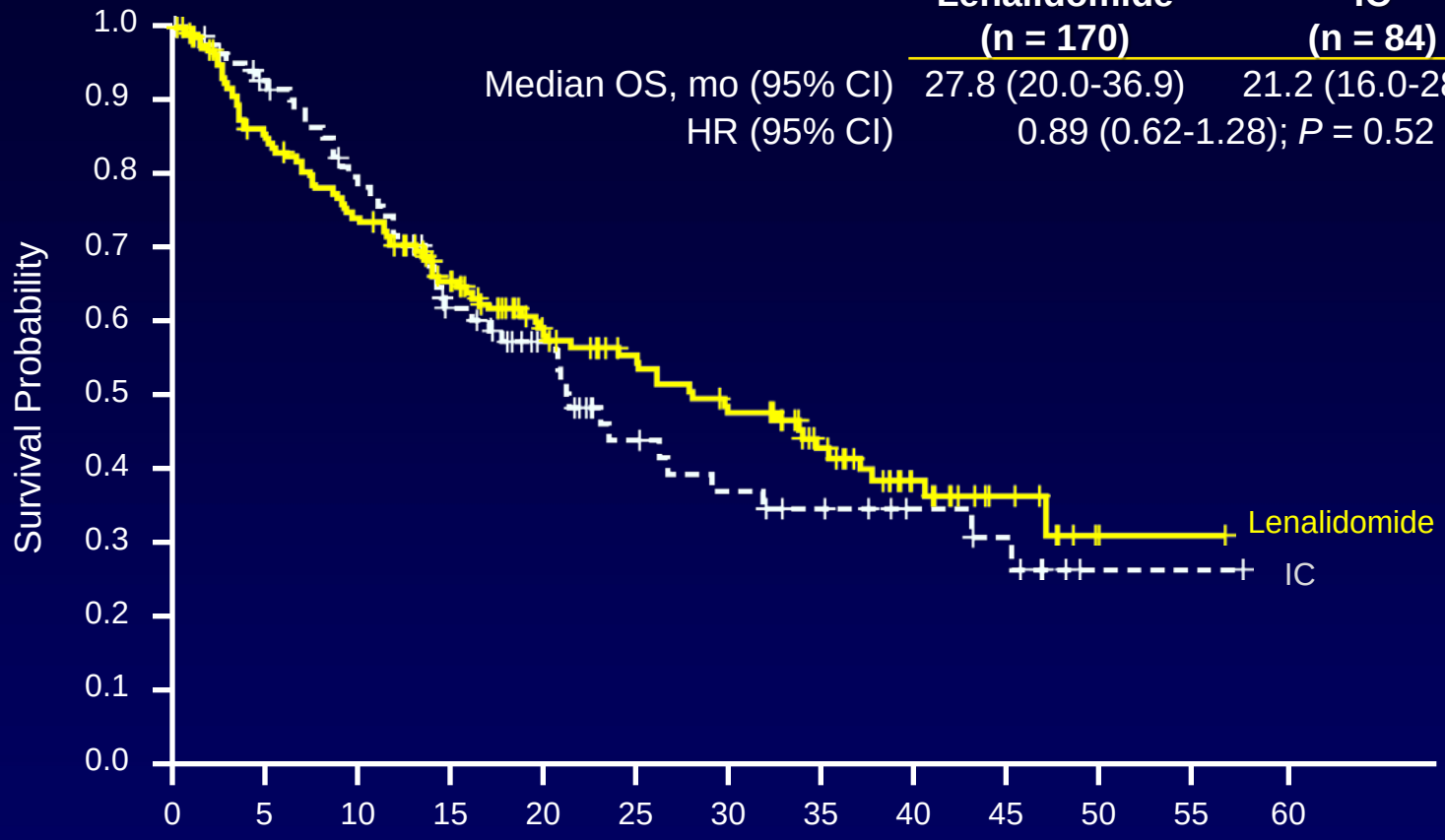
- For 39 patients who crossed over from IC to lenalidomide, best responses included 2 (5%) CR, 4 (10%) PR, 3 (8%) SD†

*Data cut-off March 7, 2014.
†No response evaluations for several patients in each arm; however, they still contributed to PFS.

Trneny M, et al. *Blood.* 2014;124: Abstract 626.

MCL-002: OS (ITT)*

	Lenalidomide (n = 170)	IC (n = 84)
Median OS, mo (95% CI)	27.8 (20.0-36.9)	21.2 (16.0-28.9)
HR (95% CI)	0.89 (0.62-1.28); *P* = 0.52	



Number of patients at risk

Lenalidomide	170	135	116	90	66	55	48	33	18	9	1	1	0
IC	84	72	59	42	32	19	16	12	9	7	1	1	0

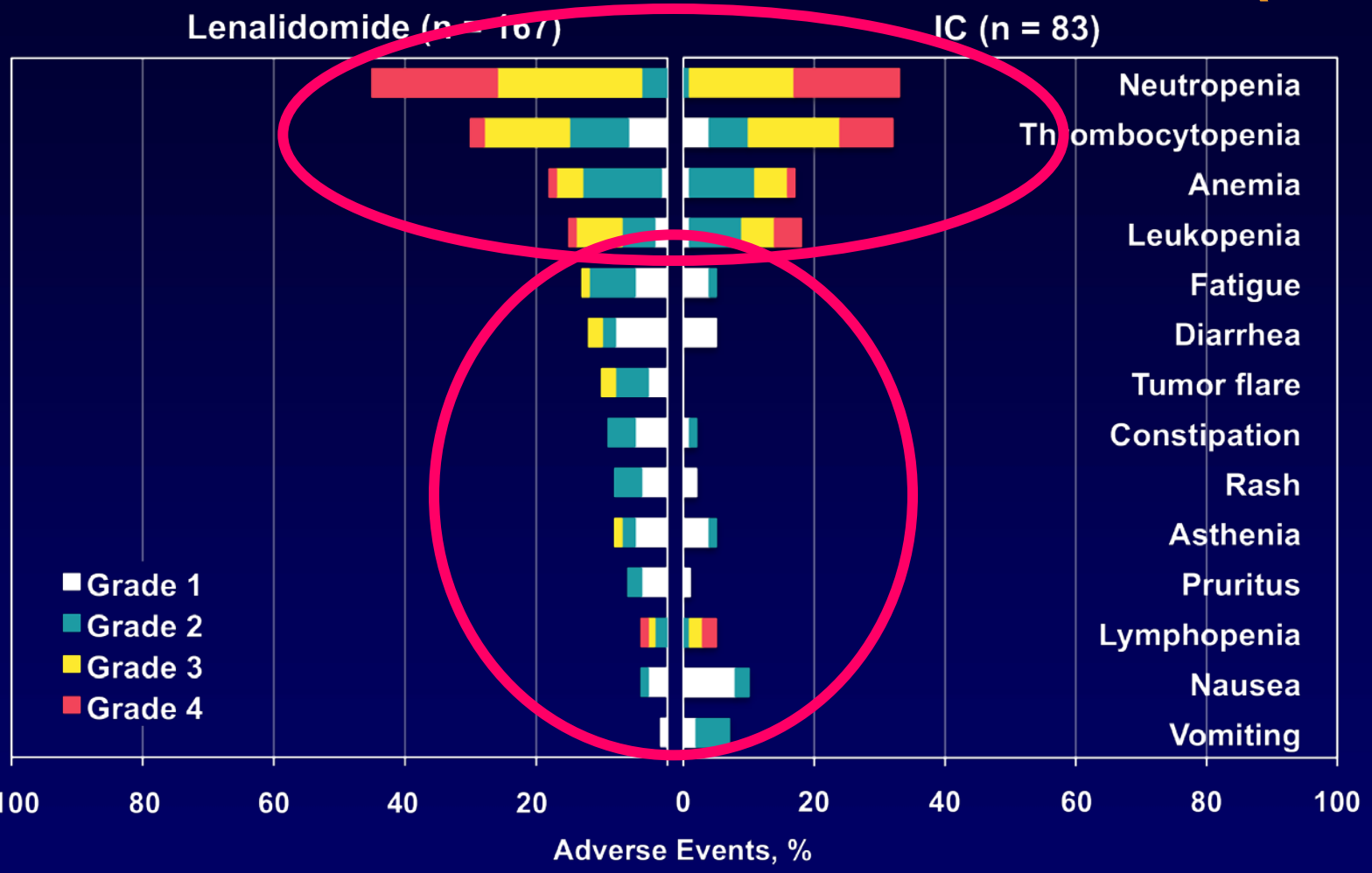
- Median follow-up time: 15.9 months
- In MCL-002, OS was not statistically powered for a direct comparison
- Crossover for patients in the IC arm with PD was 47%†

Trneny M, et al. *Blood.* 2014;124: Abstract 626.

*Data cut-off March 7, 2014. †Based on safety population.

Safety

MCL-002: Treatment-Related AEs (≥5%)*



- Median treatment duration was 24.3 weeks for lenalidomide vs 13.1 weeks for IC
- Lenalidomide-treated patients showed more dose reductions vs IC (41% vs 17%), due in part to longer median duration and strict dose modification rules for lenalidomide

*Safety analyses were performed in all patients who received ≥1 dose of treatment with a data cut-off March 7, 2014.

Trneny M, et al. *Blood.* 2014;124: Abstract 626.

MCL-002: Grade 3/4 Treatment-Related AEs (≥5%)*

Grade ≥3 AE, n (%)	Lenalidomide (n = 167)	IC (n = 83)
Neutropenia	73 (**44**)	28 (**34**)
Thrombocytopenia	30 (**18**)	23 (**28**)
Anemia	14 (**8**)	6 (**7**)
Leukopenia	13 (**8**)	9 (**11**)
Febrile neutropenia	10 (**6**)	2 (**2**)
Lymphopenia	2 (**1**)	5 (**6**)

*Safety analyses were performed in all patients who received ≥1 dose of treatment with a data cut-off March 7, 2014.

Trneny M, et al. *Blood.* 2014;124: Abstract 626.

MCL-002: Adverse Events of Interest

- Thromboembolic events occurred in 11 % of lenalidomide patients and 1% of IC patients
- Tumor flare reaction occurred in 10% of lenalidomide patients (2% grade ≥3)
- 1 patient in each arm experienced tumor lysis syndrome
- Invasive second primary malignancies were identified in 4% of lenalidomide and 5% of IC-treated patients

Trneny M, et al. *Blood.* 2014;124: Abstract 626.

Conclusions

MCL-002: Conclusions

- **MCL-002 was the first randomized, controlled study of lenalidomide vs IC in patients with R/R MCL**

Trneny M, et al. *Blood.* 2014;124: Abstract 626.

MCL-002: Conclusions

- MCL-002 was the first randomized, controlled study of lenalidomide vs IC in patients with R/R MCL
- Lenalidomide showed significantly improved PFS over IC monotherapy in patients with advanced R/R MCL
  - 39% risk reduction in disease progression or death (HR = 0.61; *P* = 0.004)
    - Median PFS = 8.7 vs 5.2 months

Trneny M, et al. *Blood.* 2014;124: Abstract 626.

MCL-002: Conclusions

- MCL-002 was the first randomized, controlled study of lenalidomide vs IC in patients with R/R MCL
- Lenalidomide showed significantly improved PFS over IC monotherapy in patients with advanced R/R MCL
  - 39% risk reduction in disease progression or death (HR = 0.61; *P* = 0.004)
    - Median PFS = 8.7 vs 5.2 months
- Responses were significantly improved for lenalidomide vs IC
  - ORR = 40% vs 11% (*P*<.001)
  - CR/CRu = 5% vs 0 (*P*<.043)

Trneny M, et al. *Blood.* 2014;124: Abstract 626.

MCL-002: Conclusions

- MCL-002 was the first randomized, controlled study of lenalidomide vs IC in patients with R/R MCL
- Lenalidomide showed significantly improved PFS over IC monotherapy in patients with advanced R/R MCL
  - 39% risk reduction in disease progression or death (HR = 0.61; *P* = 0.004)
    - Median PFS = 8.7 vs 5.2 months
- Responses were significantly improved for lenalidomide vs IC
  - ORR = 40% vs 11% (*P*<.001)
  - CR/CRu = 5% vs 0 (*P*<.043)
- Lenalidomide had a good safety profile

Trneny M, et al. *Blood.* 2014;124: Abstract 626.

MCL-002: Conclusions

- MCL-002 was the first randomized, controlled study of lenalidomide vs IC in patients with R/R MCL
- Lenalidomide showed significantly improved PFS over IC monotherapy in patients with advanced R/R MCL
  - 39% risk reduction in disease progression or death (HR = 0.61; *P* = 0.004)
    - Median PFS = 8.7 vs 5.2 months
- Responses were significantly improved for lenalidomide vs IC
  - ORR = 40% vs 11% (*P* < 0.001)
  - CR/CRu = 5% vs 0 (*P* < 0.043)
- Lenalidomide had a good safety profile
- **Lenalidomide showed superior efficacy and positive benefit : risk ratio in these patients**

Trneny M, et al. *Blood.* 2014;124: Abstract 626.