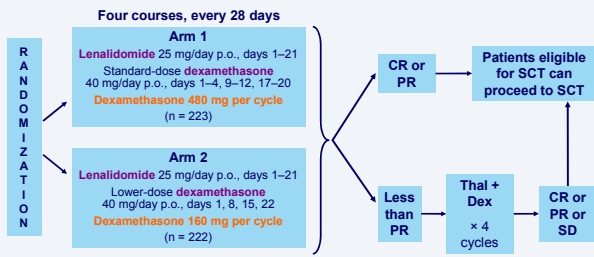


The role of novel agents in front-line therapy: Lenalidomide

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ECOG-E4A03: Len + standard- or low-dose Dex in newly diagnosed MM

Phase III, randomized study in newly diagnosed MM
(N = 445)



Rajkumar SV, et al. J Clin Oncol. 2008;26 [abstract 8504].

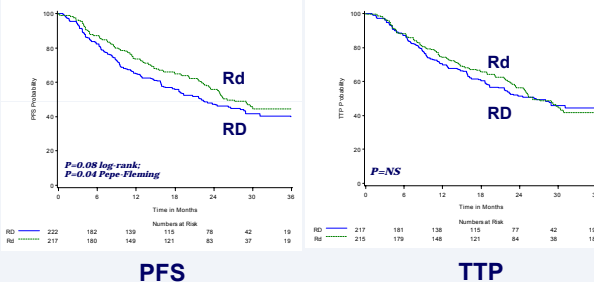
ECOG-E4A03: fewer adverse events with low-dose than with standard-dose Dex

Grade 3 or 4 adverse event	Len + standard-dose Dex, % (n = 223)	Len + low-dose Dex, % (n = 220)	p value
Infection or pneumonia	16	8	0.019
DVT or PE	25	11	< 0.001
Neuropathy	2	2	0.999
Cardiac ischaemia	3	0.5	0.068

Rajkumar SV, et al. J Clin Oncol. 2008;26 [abstract 8504].
Updated data presented at ASCO Annual Meeting, 2008.

PE = pulmonary embolism.

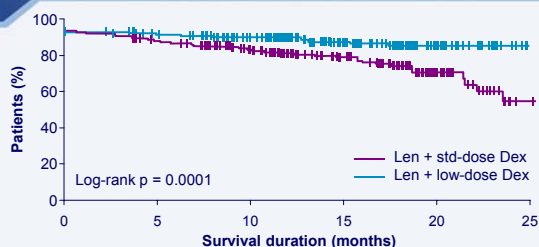
ECOG-E4A03: PFS and TTP



PFS

TTP

ECOG-E4A03: overall survival rate better with low- than with standard-dose Dex



	n	Event, % (n)	Censored, % (n)	Median survival (95% CI)
Len + std-dose Dex	223	18 (41)	82 (182)	NR (23.56-NR)
Len + low-dose Dex	222	6 (13)	94 (209)	NR

Overall survival was significantly better in the low-dose Dex arm (p < 0.001)

NR = not reached.

Rajkumar SV, et al. J Clin Oncol. 2007;25:18S [abstract LBA8025].

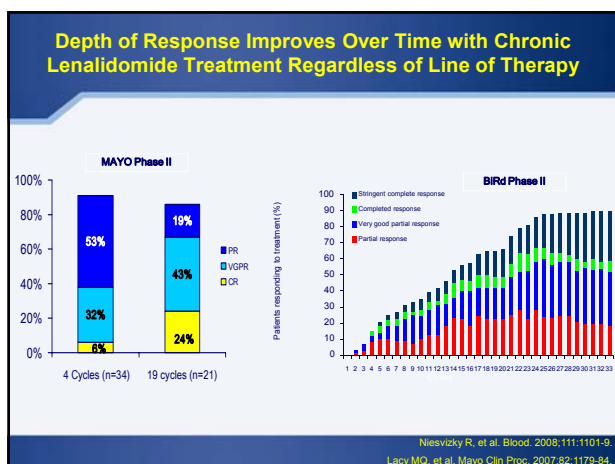
ECOG-E4A03: 2-year survival rate by patient age; low- vs standard-dose Dex

	Number of patients	2-Year survival probability (95% CI)
Age < 65 years		
Len + standard-dose Dex	104	0.85 (0.78-0.93)*
Len + low-dose Dex	108	0.91 (0.84-0.98)*
Age ≥ 65 years		
Len + standard-dose Dex	119	0.67 (0.56-0.77)†
Len + low-dose Dex	114	0.82 (0.74-0.91)†

*p = 0.16.

†p = 0.009.

Rajkumar SV, et al. J Clin Oncol. 2007;25:18S [abstract LBA8025].
Rajkumar SV, et al. Blood. 2007;110:[abstract 74].



MM-020: lenalidomide + low-dose Dex vs MPT in previously untreated MM

Inclusion criteria

- Previously untreated MM
- Age ≥ 65 years or not a candidate for transplantation
- No neuropathy of grade > 2
- CL_{Cr} > 30 ml/min

Arms:

- Arm 1:** Lenalidomide 25 mg/day, days 1–21; every 28 days + Dexamethasone* 40 mg/day, days 1, 8, 15, 22; every 28 days → Until PD
- Arm 2:** Lenalidomide 25 mg/day, days 1–21; every 28 days + Dexamethasone* 40 mg/day, days 1, 8, 15, 22; every 28 days → Eighteen 4-week cycles or until PD
- Arm 3:** Melphalan* 0.25 mg/kg/day, days 1–4, every 42 days + Prednisone 2.0 mg/kg/day, days 1–4, every 42 days + Thalidomide* 200 mg/day, daily through 42-day cycle → Twelve 6-week cycles or until PD

N = 1,590
Centres in EU, Switzerland, USA, and Canada

* In patients older than 75 years
• Dexamethasone 20 mg/day
• Melphalan 0.20 mg/kg/day
• Thalidomide 100 mg/day

Calgene Corporation. Protocol CC-5013-MM-020/IFM 07-01; 2007. Data on file.
CL_{Cr} = creatinine clearance rate.

Phase I and II trial of MPR in newly diagnosed MM

Median age 71 (range 57–77) years

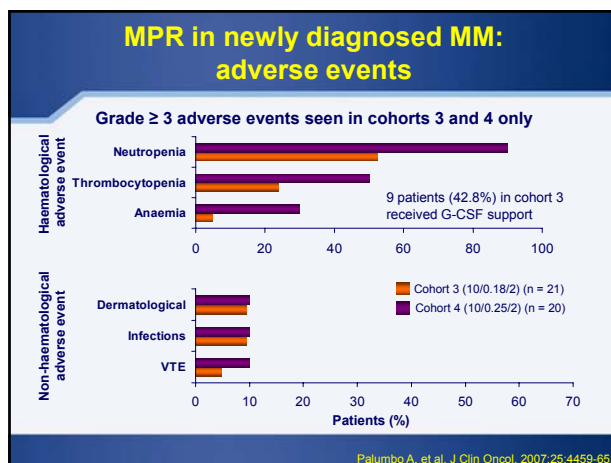
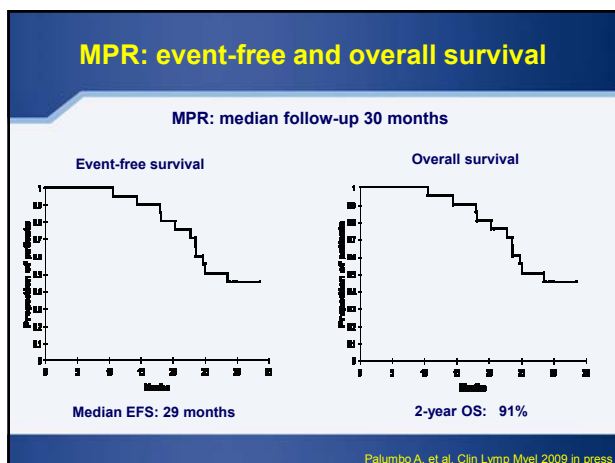
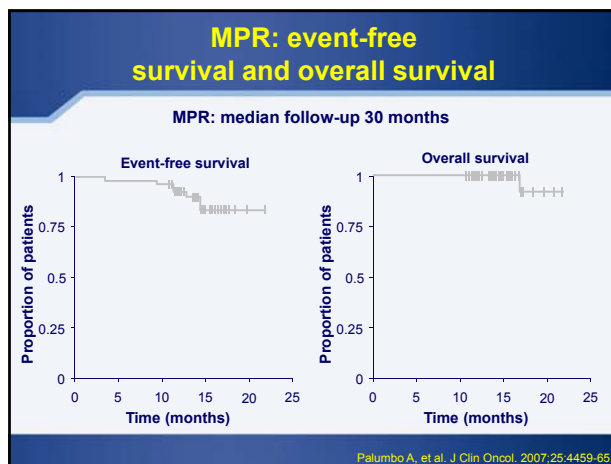
Cohort	Lenalidomide (mg/day)	Melphalan (mg/kg/day)	Prednisone (mg/kg/day)
1 (n = 6)	5	0.18	2
2 (n = 6)	5	0.25	2
3 (n = 6 + 15)	10	0.18	2
4 (n = 6 + 15)	10	0.25	2

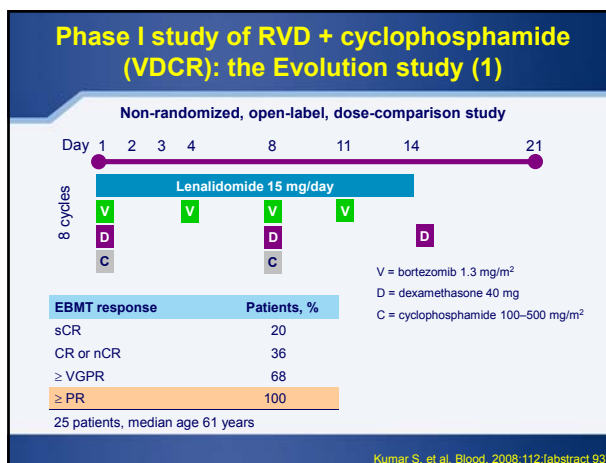
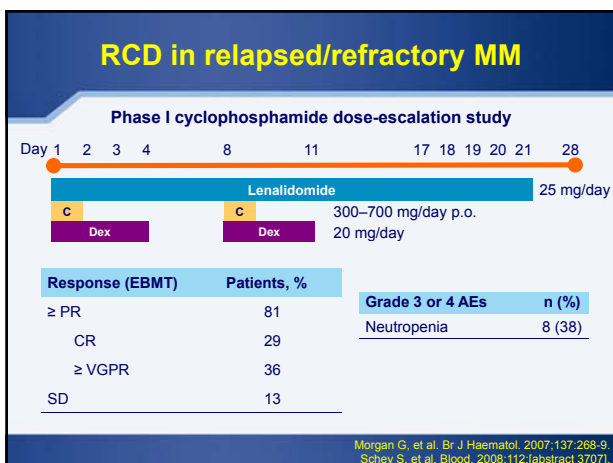
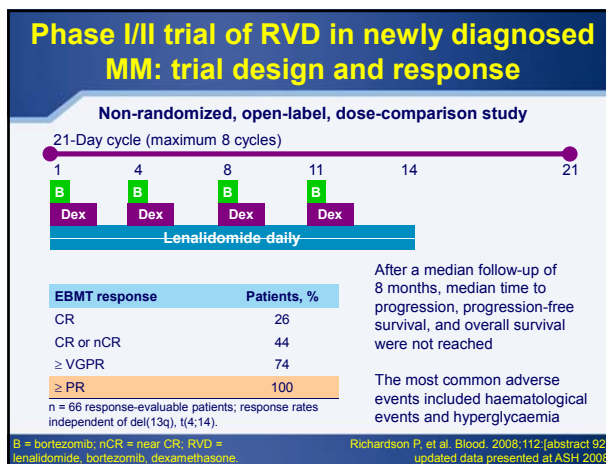
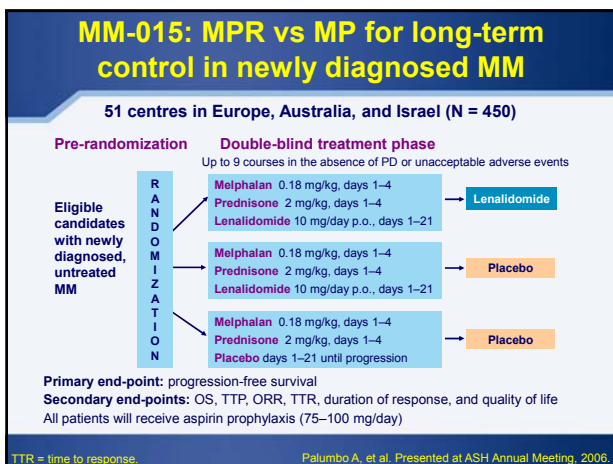
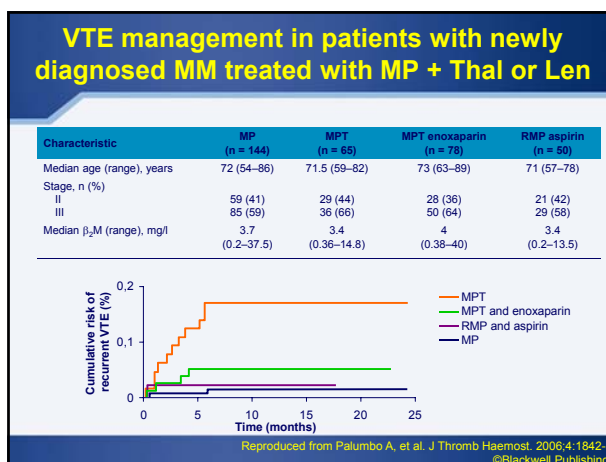
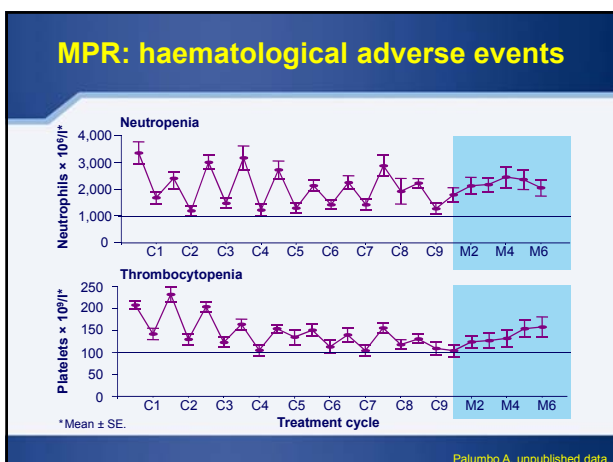
Day 1 2 3 4 21

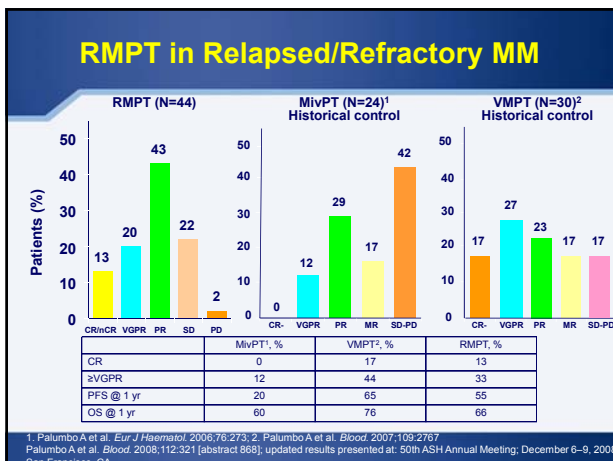
Legend: ■ Lenalidomide, ■ Melphalan, ■ Prednisone

Every 4–6 weeks for maximum of 9 cycles
Aspirin (100 mg/day) given as VTE prophylaxis

MPR = MP + lenalidomide. Palumbo A, et al. Haematologica. 2007;92 Suppl 2:179.







- ### Conclusion
- MPR: future standard of care
 - Rd: alternative long term treatment
 - CRD: alternative alkylating agent
 - VCRD- RMPT: research 4 drug approach