

Highlights from EHA

Report dei gruppi di lavoro >>
[Mieloma multiplo]

Relatore: **M.T. PETRUCCI**

27-28 ottobre 2008

Borgo S. Luigi – Monteriggioni (Siena)

Gruppo di lavoro

2

[Mieloma multiplo]

ANTONINO BAGNATO

ALESSANDRO LUCCHESI

BENEDETTA BARTOLOZZI

ANDREA NOZZA

SILVIA BUTTIGNOL

ALESSANDRO POLACCO

EMILIA COCOROCCHIO

ERMINIA RINALDI

ANTONIO LAZZARO

Highlight from EHA Borgo San Luigi 27-10-2008

3

Risultati del gruppo di lavoro:

Commento generale: difficoltà ad ottenere i nuovi farmaci

Trattamento di prima scelta in prima linea:

Giovani

autologo

- induzione TD
- trapianto 2 se non RC
- mantenimento con Thal 50 mg 2 centri

4

Discussione

Trattamento di prima scelta in prima linea

5

Anziani

Terapie registrate: VMP, MPT (MPR in valutazione)

Gruppo di Lavoro → MPT

6

Discussione

Trattamento di prima scelta prima recidiva

7

Registrati: Velcade monoterapia; Lenalidomide Dex; Velcade Doxyl

Gruppo di Lavoro:

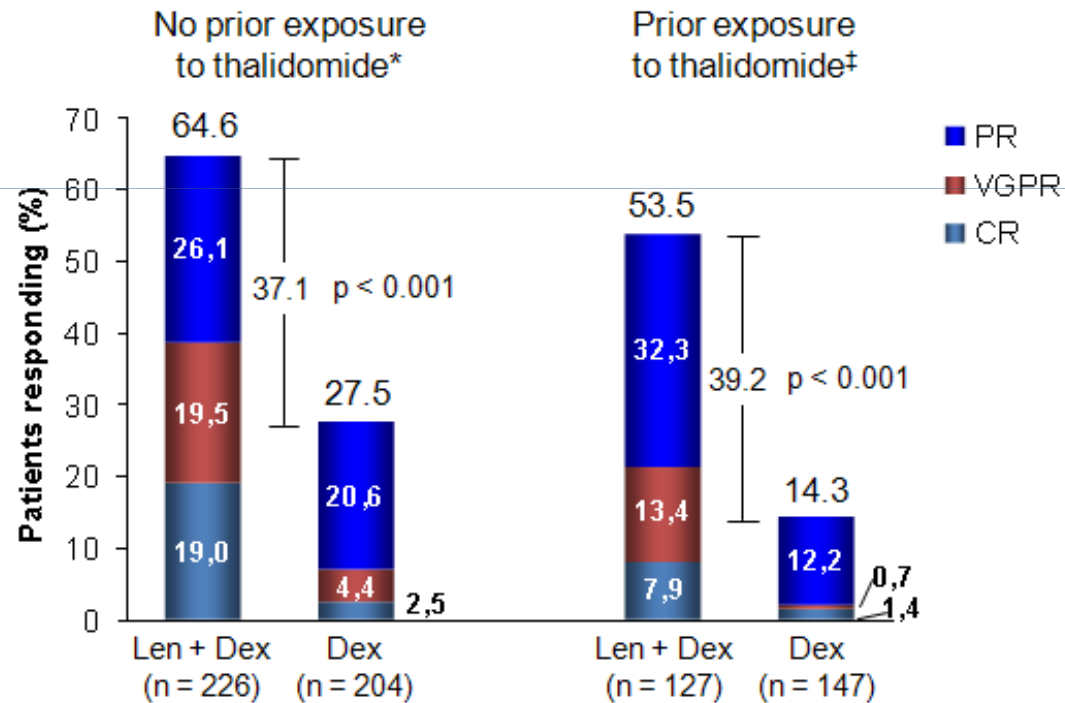
Prima scelta Velcade:

1. Esperienza (**2 centri in EAP usano Len**)
2. precedente terapia con Thal
3. In insufficienza renale 100% usa Velcade (conoscono linee guida Lenalidomide)
4. 1 centro usa VTD
5. Usato anche Doxyl (dopo non risposta con Vel)

Lenalidomide is effective after prior exposure to thalidomide

8

MM-009 and MM-010: prospective subgroup analysis of patients with relapsed/refractory MM



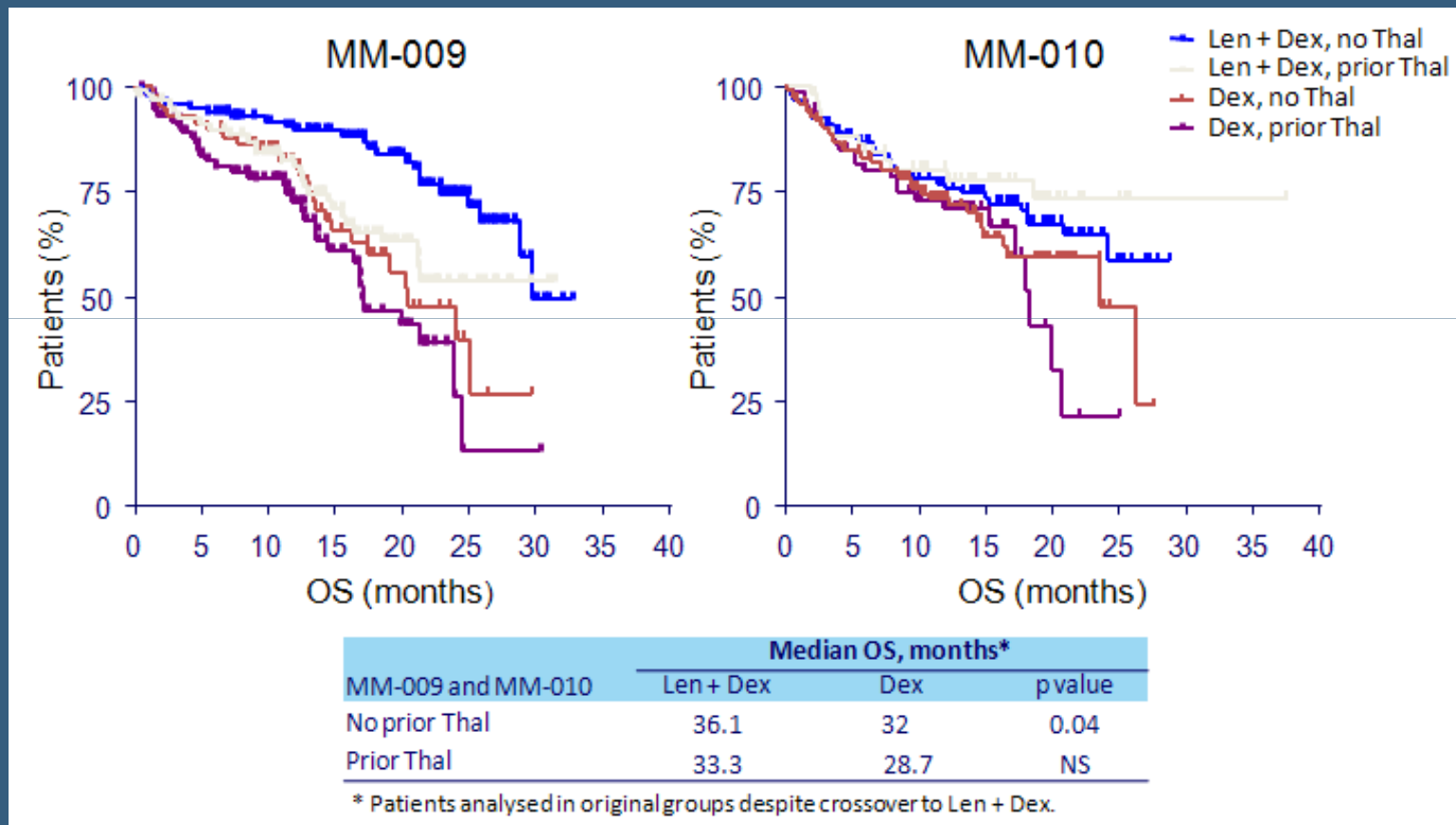
*Median 2 prior lines of treatment.

†Median 3 prior lines of treatment.

Wang M, et al. Blood. In press 2008.

MM-009 and MM-010: increased OS with Len + Dex regardless of prior Thal

9



Dimopoulos M, et al. N Engl J Med. 2007;357:2123-32.

Wang M, et al. Blood. In press 2008. Weber DM, et al. N Engl J Med. 2007;357:2133-42.

Len + Dex more effective than Dex despite thalidomide resistance

10

MM-009 and MM-010: prospective subgroup analysis

	T1 (n = 124)		T2 (n = 65)		T3 (n = 44)	
	Len + Dex (n = 54)	Dex (n = 70)	Len + Dex (n = 31)	Dex (n = 34)	Len + Dex (n = 20)	Dex (n = 24)
ORR, %	65	17	42	6	50	21
CR	11	1	7	3	5	0
VGPR	13	1	13	3	20	0
PR	41	14	23	0	25	21
Median TTP, months	9.3	4.6	7.8	3.7	7.2	3.7

All differences between Len + Dex and Dex: $p < 0.05$.

T1 (thalidomide sensitive): responded to thalidomide; no progression during thalidomide therapy

T2 (thalidomide relapsed): responded to thalidomide; progressed during thalidomide therapy

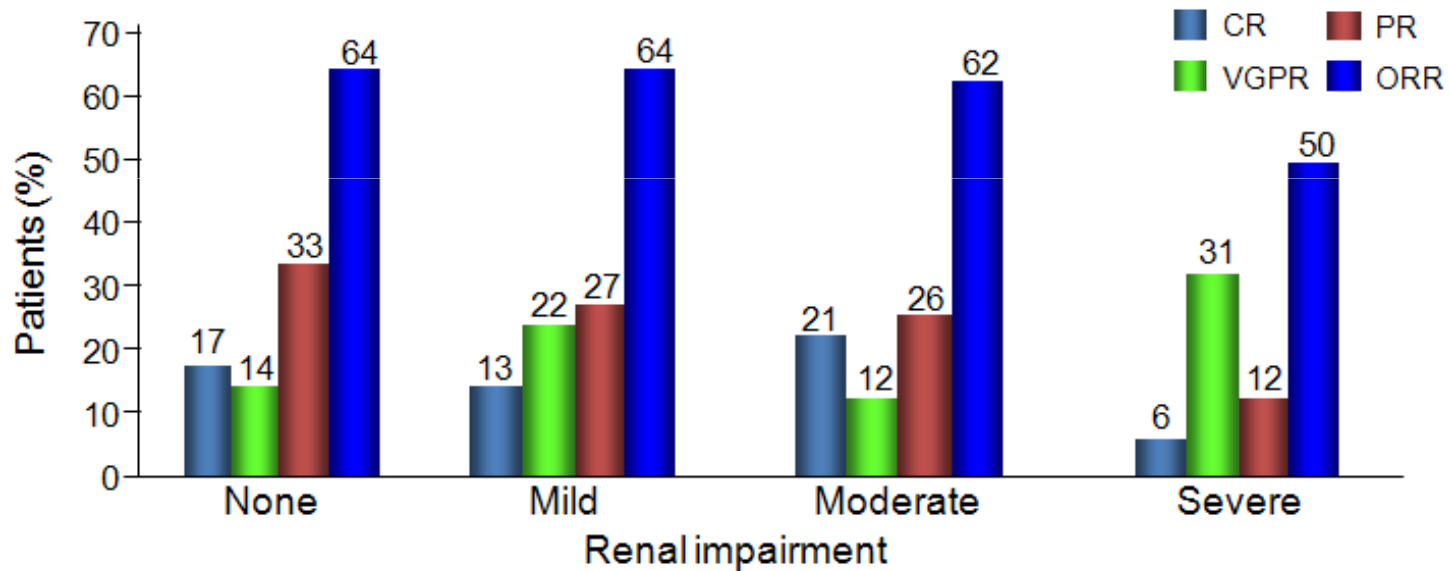
T3 (thalidomide refractory): no response to thalidomide; progressed during thalidomide therapy

Wang M, et al. Blood. In press 2008.

Len + Dex is effective regardless of renal insufficiency

11

MM-009 and MM-010: prospective subgroup analysis of MM patients with renal insufficiency



	None (CL _{Cr} > 80 ml/min)	Mild (50 ≤ CL _{Cr} ≤ 80 ml/min)	Moderate (30 ≤ CL _{Cr} < 50 ml/min)	Severe (CL _{Cr} < 30 ml/min)
Median TTP, months	11.3	12.1	11.4	7.9

CL_{Cr} = creatinine clearance rate.

Weber D, et al. J Clin Oncol. 2008;26:[abstract 8542].

Lenalidomide can be safely used in patients with renal insufficiency

12

In patients with severe renal impairment, adverse events should be actively managed

Adverse events, %	Degree of renal impairment			
	None (n = 158)	Mild (n = 125)	Moderate (n = 42)	Severe (n = 16)
Neutropenia	31	39	43	38
Thrombocytopenia	7	16*	19*	38**
Thrombotic events	11	12	14	6

*p < 0.05 versus no renal impairment; **p < 0.001 versus no renal impairment.

Of 174 patients with renal insufficiency, 119 (68%) had improvement in their renal function by at least one level within 4 months, as assessed by peak creatinine clearance rate

Weber D, et al. J Clin Oncol. 2008;26:[abstract 8542].

Recommended lenalidomide dose adjustments in case of renal impairment

13

Renal impairment	Dosage
Mild ($CL_{Cr} \geq 50$ ml/min)	25 mg daily
Moderate ($30 \leq CL_{Cr} < 50$ ml/min)	10 mg daily*
Severe ($CL_{Cr} < 30$ ml/min and dialysis not needed)	15 mg every 48 hours
End-stage renal disease ($CL_{Cr} < 30$ ml/min and dialysis needed)	15 mg 3 times a week after each dialysis

*The dose may be increased to 15 mg daily after 2 cycles if patient has no response to treatment.

Chen N, et al. J Clin Pharmacol. 2007;47:1466.

14

Discussione

Filosofia di trattamento

15

100% del gruppo preferisce un trattamento sequenziale

Trattamento con Lenalidomide

70-80 % usa dosi ridotte di Desametasone (soprattutto anziani)

Dex dose adjustment improves efficacy and tolerability in patients with relapsed/refractory MM (1)

16

MM-009 and MM-010: subanalysis

	Len + Dex		p value
	Dex unchanged (n = 177)	Dex reduced (n = 46)*	
Response, %			
OR	50.8	69.6	< 0.05
CR	13.0	23.9	< 0.01
nCR	19.8	37.0	< 0.01
PR	18.1	8.7	< 0.01
Adverse events grade 3 or 4, %			
Neutropenia	32.6	23.7	
Thrombocytopenia	6.8	8.5	
Anaemia	6.2	6.8	

* Dex dose reductions were 40 mg/day, days 1–4, every 2 weeks (level –1); 40 mg/day, days 1–4, every 4 weeks (level –2); and 20 mg/day, days 1–4, every 4 weeks (level –3).

San Miguel JF, et al. Blood. 2007;110:[abstract 2712].

17

Discussione