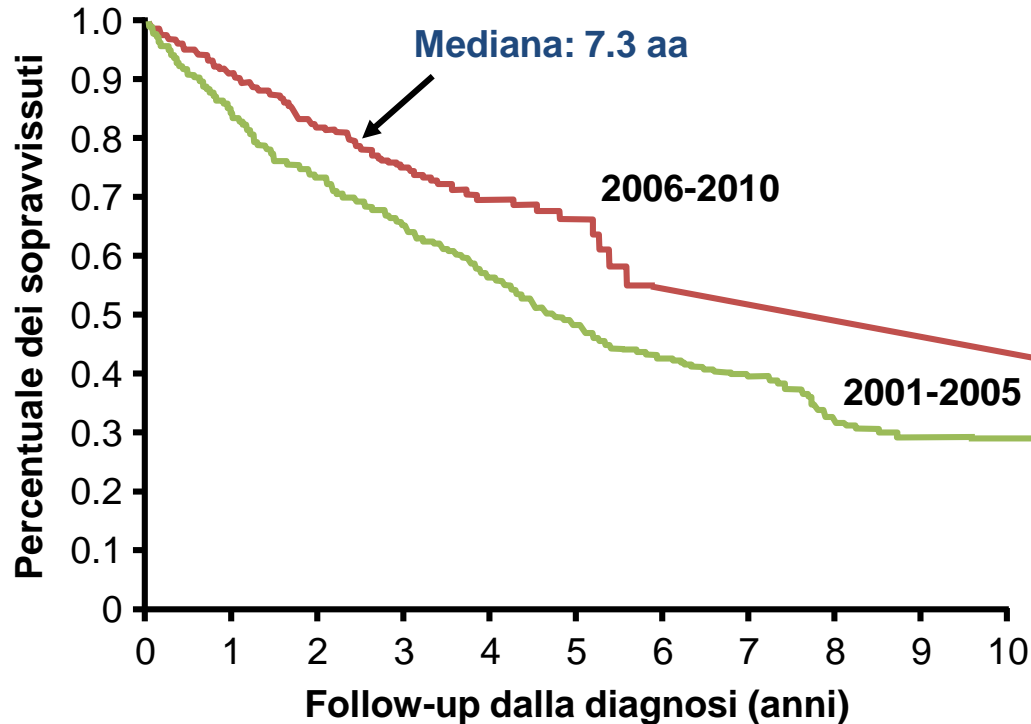


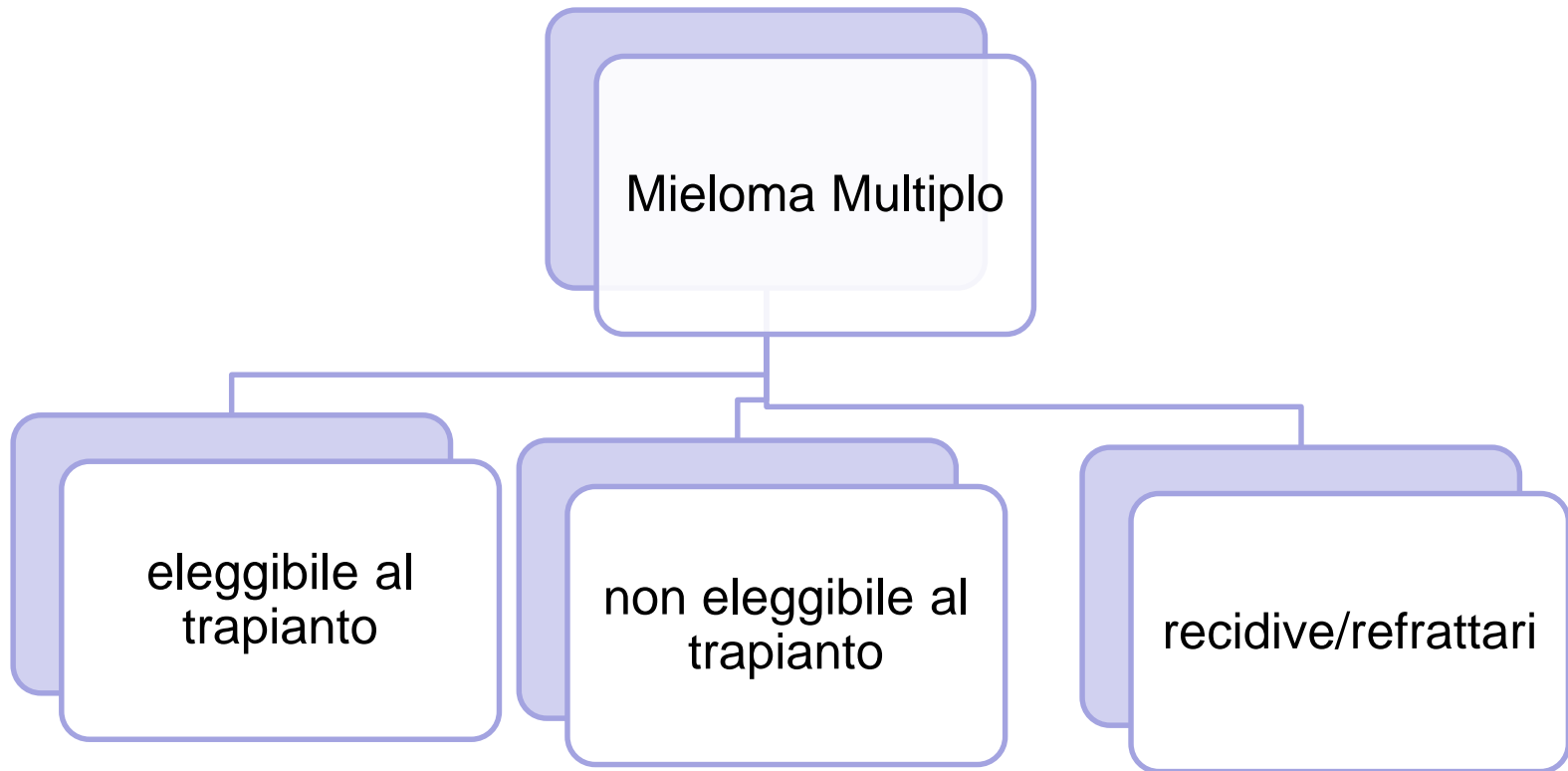
Mieloma Multiplo

MM: Sopravvivenza più lunga utilizzando i nuovi farmaci

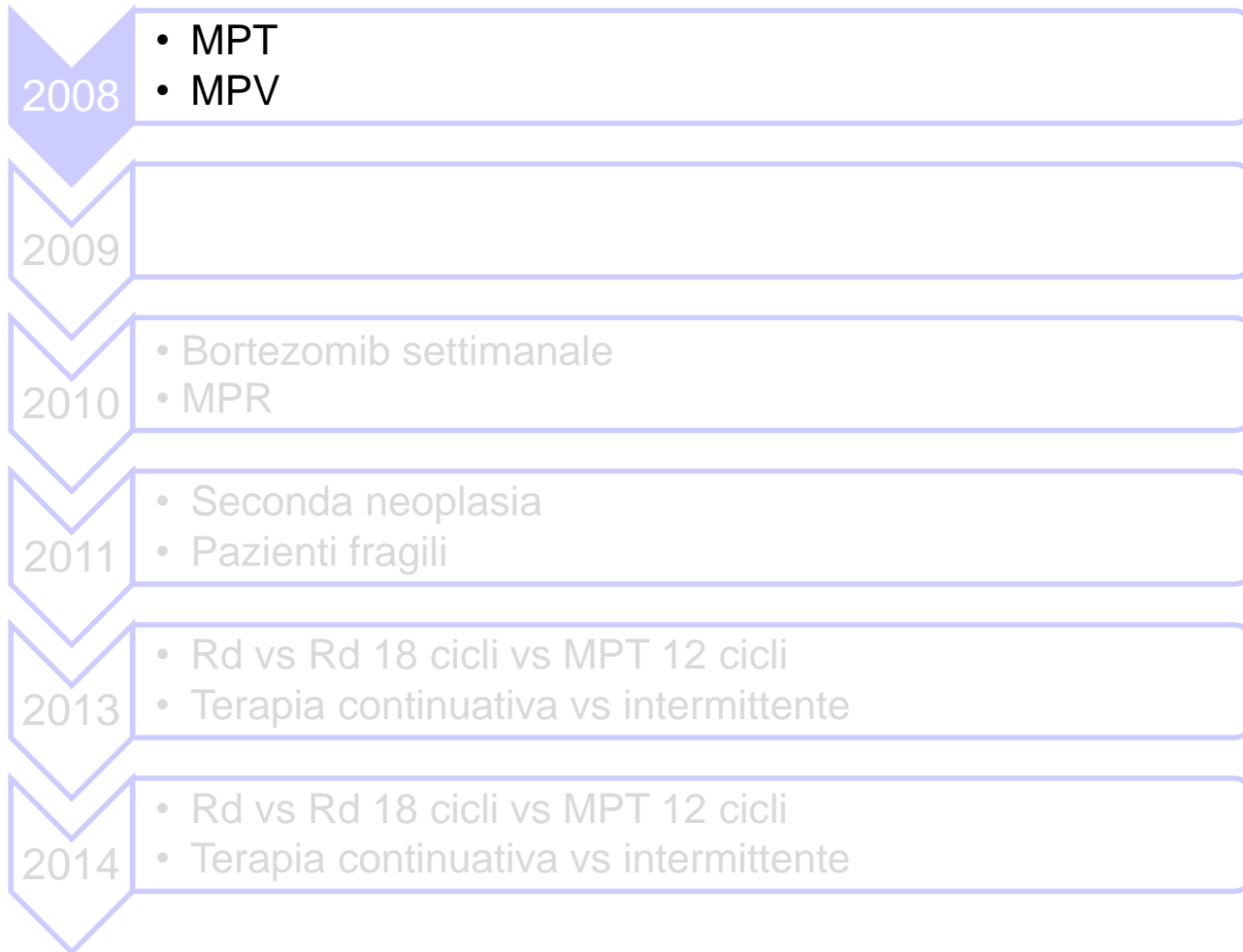


Sopravvivenza mediana a 5 anni

	≤ 65 aa	> 65 aa
2006-2010	73 %	56 %
2001-2005	63 %	31 %



pazienti non eleggibili per il trapianto



pazienti non eleggibili per il trapianto

Nuovi Standard

MPT

(Melfalan, Prednisone, Talidomide)

approvato per pazienti
di nuova diagnosi non
elegibili per le alte dosi
di chemioterapia

età \geq 65 anni

Italia: Marzo 2009

MPV

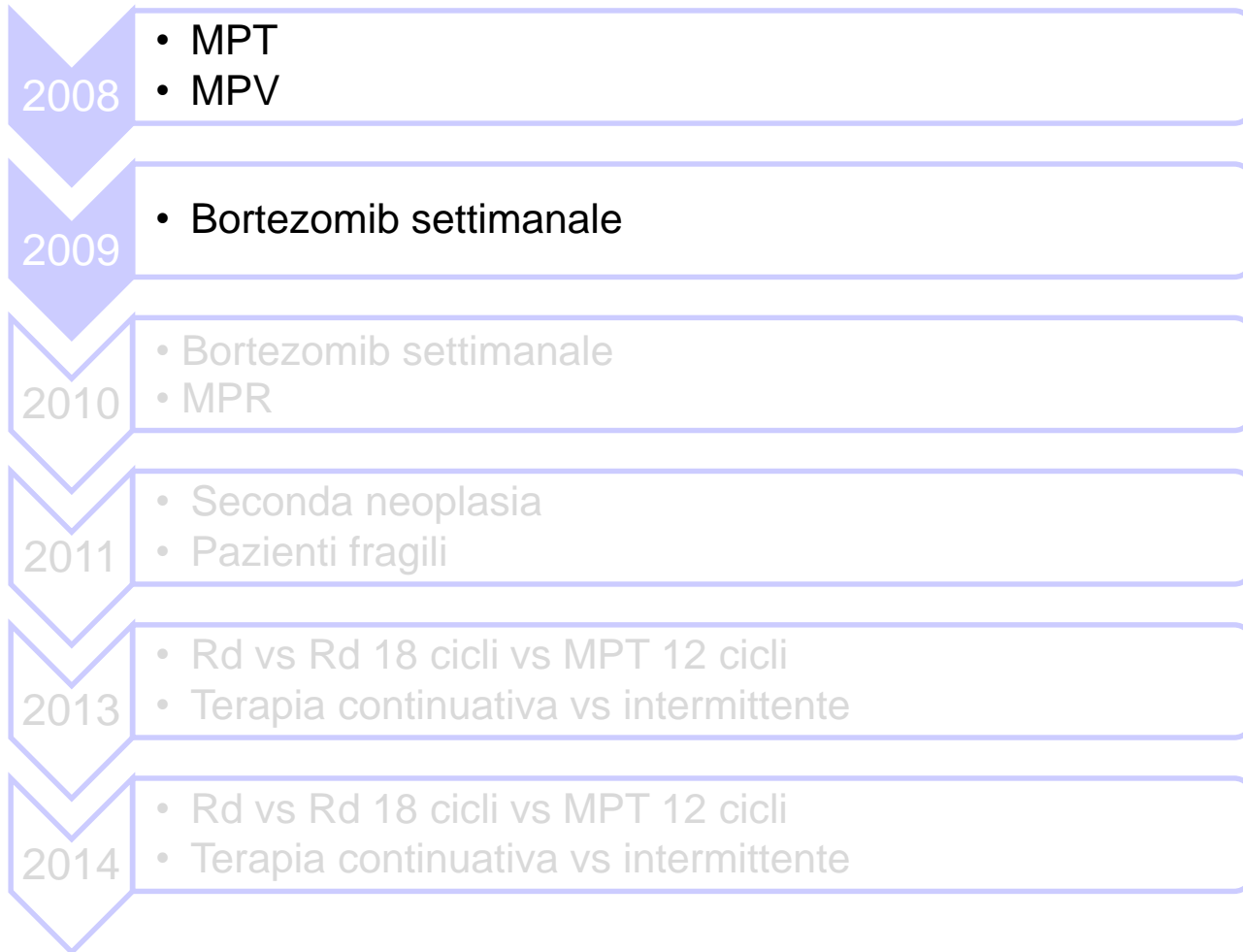
(Melfalan, Prednisone, Velcade)

approvato per pazienti
di nuova diagnosi non
elegibili per le alte dosi
di chemioterapia

età \geq 65 anni

Italia: Luglio 2009

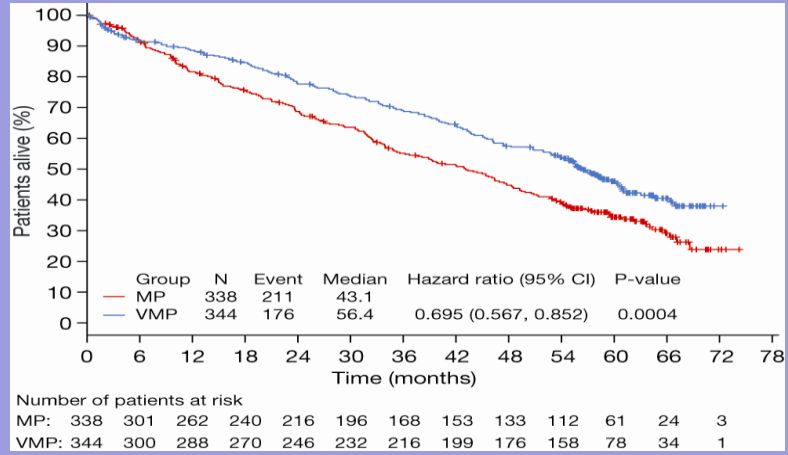
pazienti non eleggibili per il trapianto



Da VMP bi-settimanale a mono-settimanale

5aa OS VISTA VMP BW

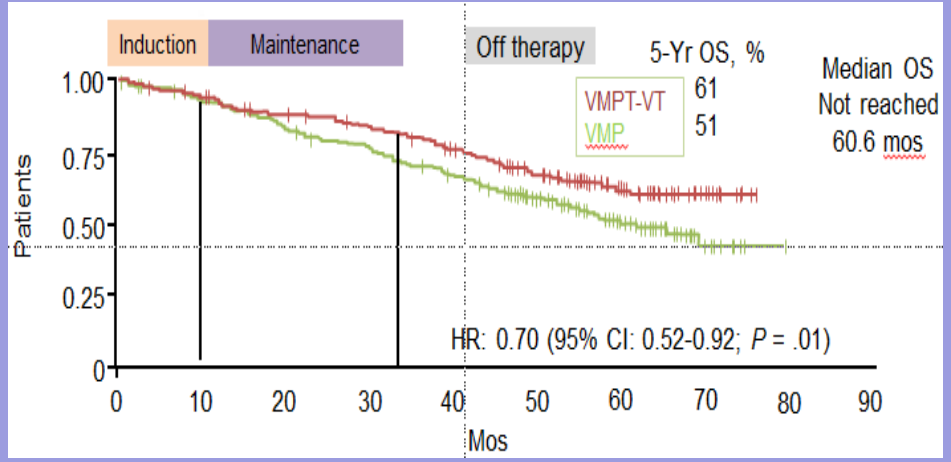
follow-up mediano 60.1 m



31% riduzione del rischio di morte

5aaOS GIMEMA VMP OW

Follow-up mediano 54 m

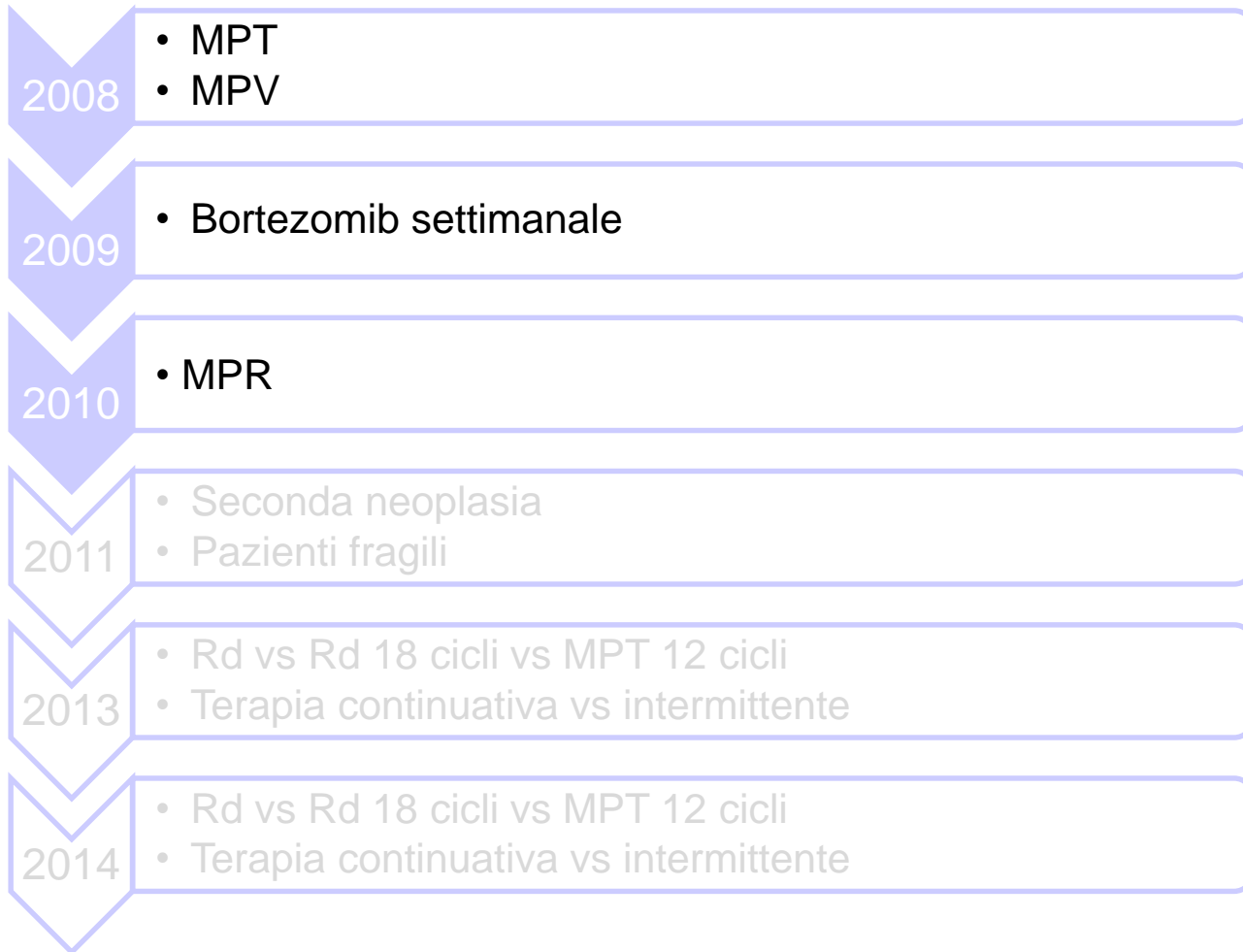


30% riduzione del rischio di morte

	VMP VISTA	VMP OW
5-anni OS (%)	46	51
mOS (m)	56,4	60,6
Dose totale pianificata, mg/m ²	67.6	46.8
Dose mediana cumulata, mg/m ²	38.5	40.3
% della dose pianificata	57	86.1

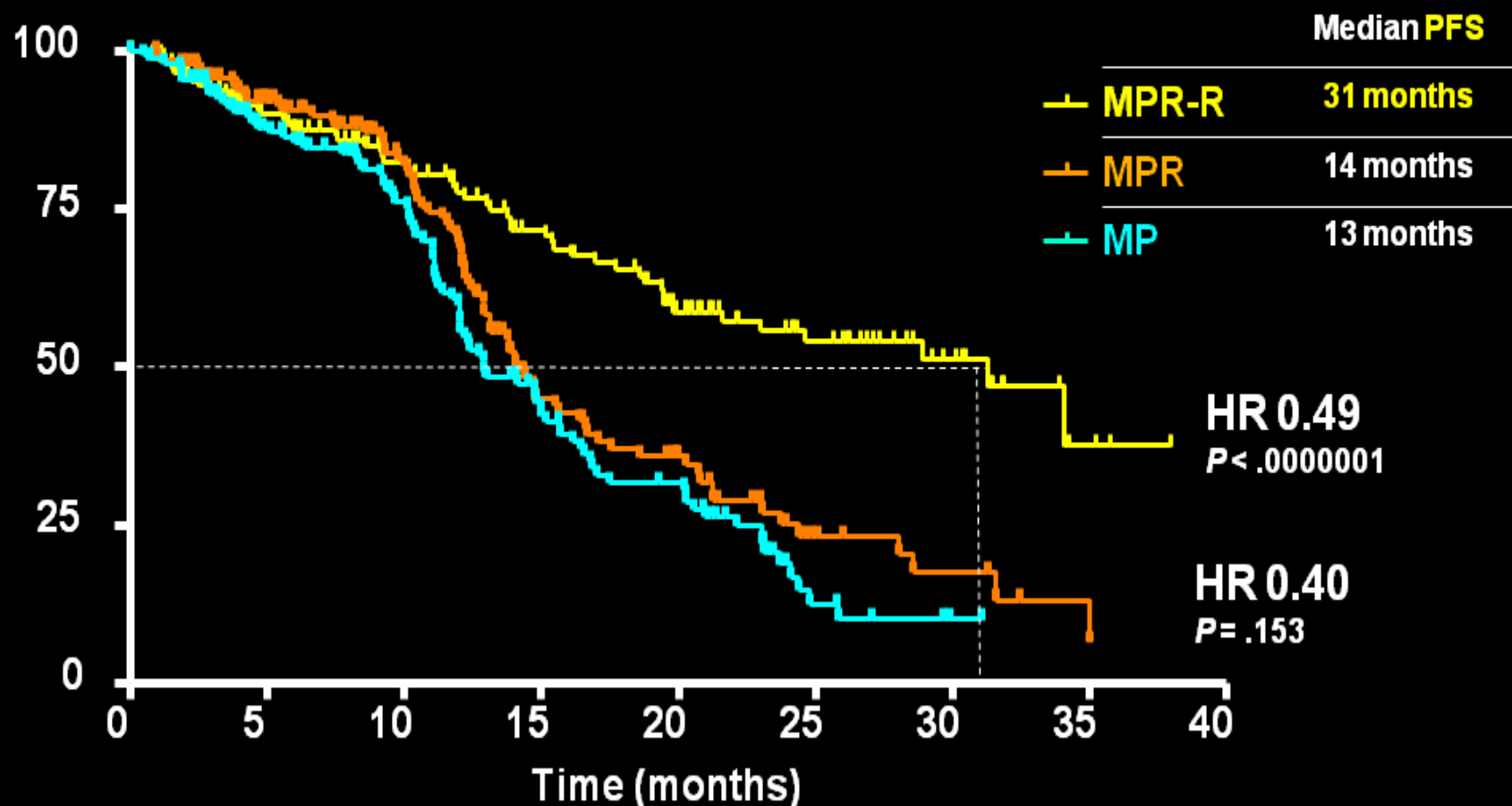
Studio	CR (IF-)	TTP, OS	PN	Interruzione
VISTA: VMP vs MP San Miguel et al. N Engl J Med 2008	VMP: 33%	TTP: 24 months OS: median not reached at 25.9 months 3-year OS: 72%	14%	14 VMP + 19% V only
VMPT vs VMP Palumbo et al. JCO 2010	VMP: 20%	Median TTP and OS not yet available VMPT: 3-year PFS 75% VMP: 3-year PFS 70%	2%	10%
VMP vs VTP Mateos et al. Lancet Oncol 2010	VMP: 22%	Median TTP and OS not yet available 2-year TTP: 72% 2-year OS: ~90%	5%	8%

pazienti non eleggibili per il trapianto



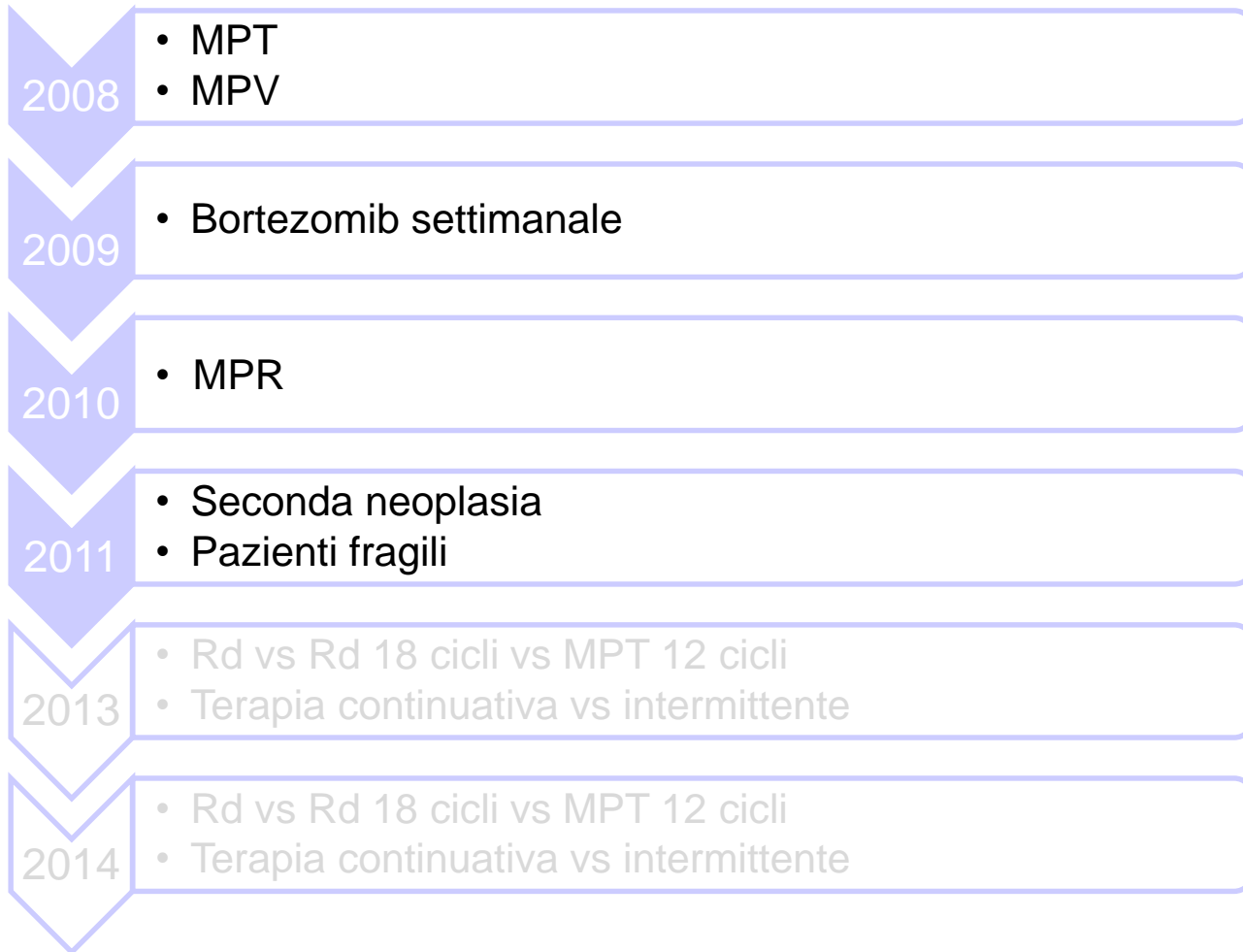
Response & PFS: **MPR-R** vs **MP** vs **MPR**

%RR (%CR): 77(10) vs 50(3) vs 68(3)



Median follow-up 30 months

pazienti non eleggibili per il trapianto

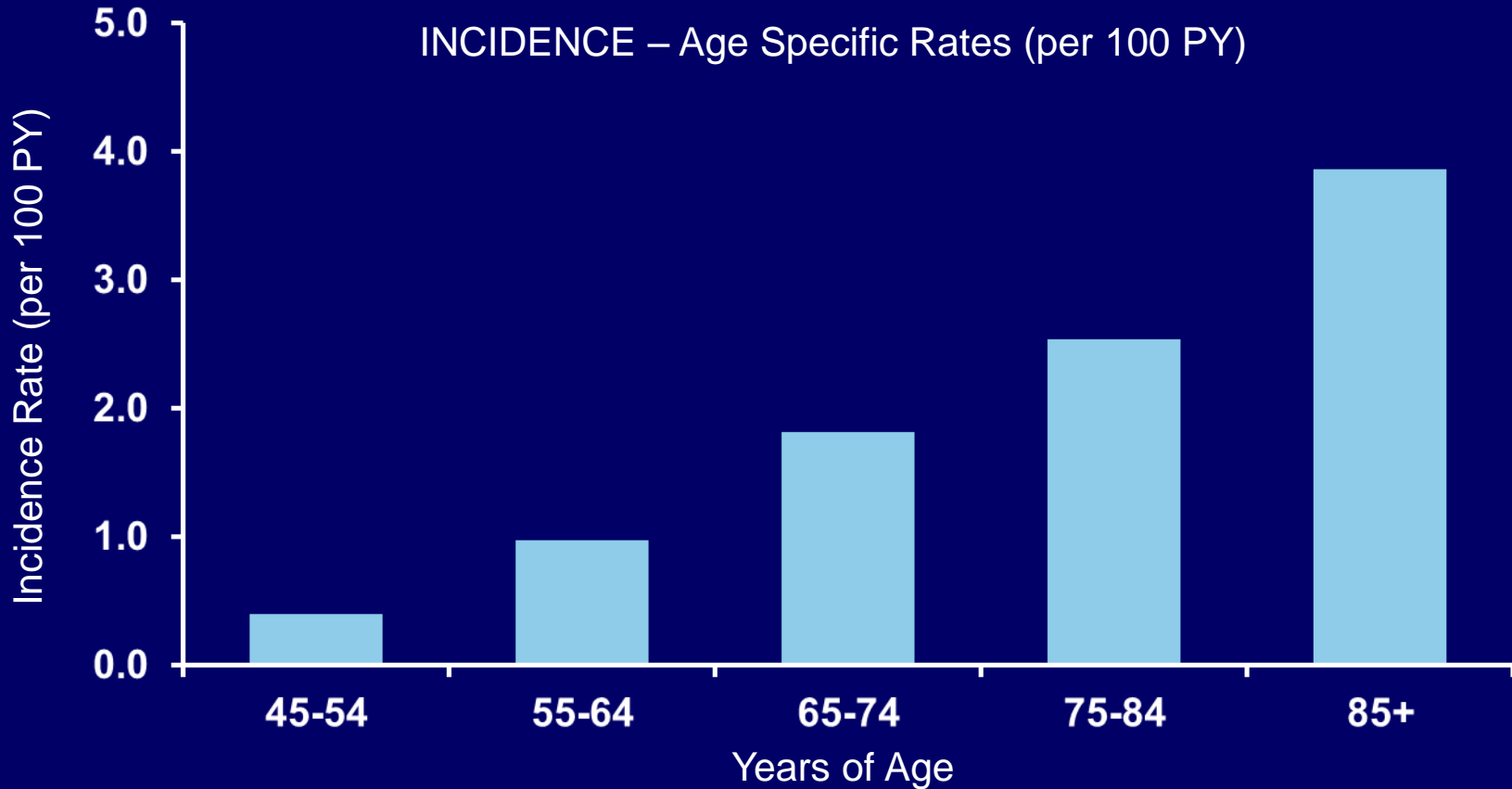


Incidence of Second Primary Malignancy

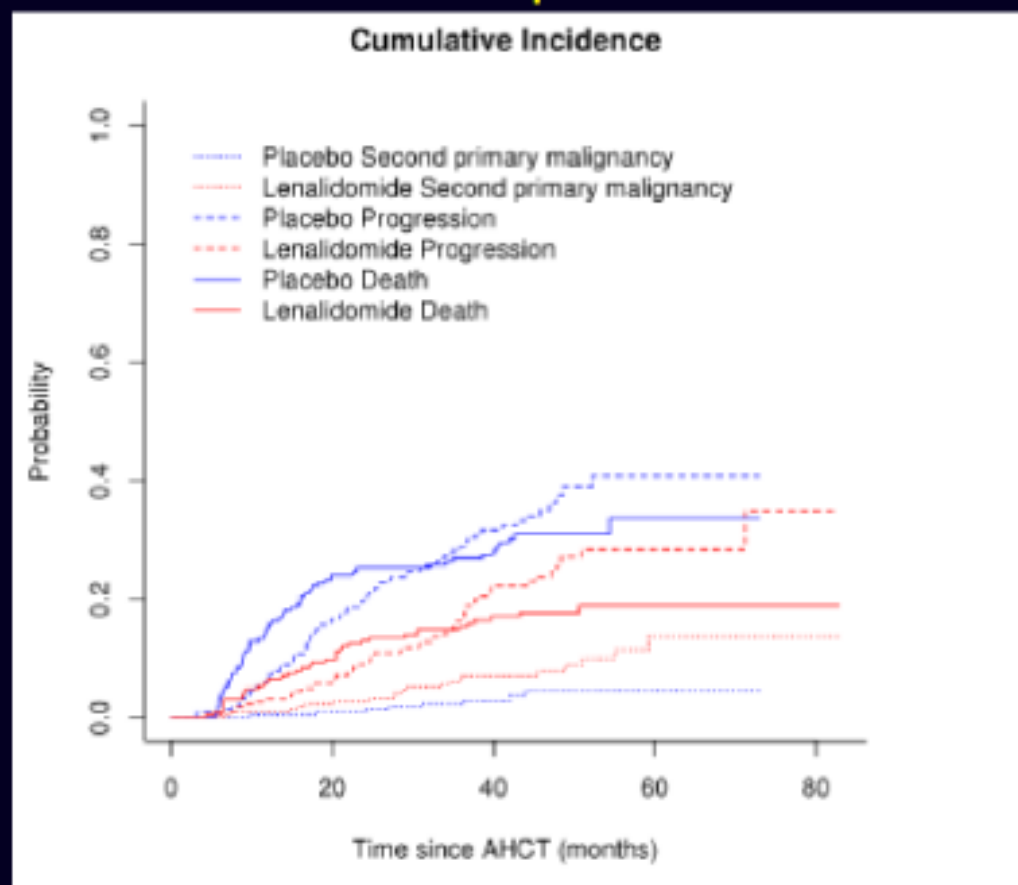
	VISTA ¹		MM015 ²		IFM2005-02 ³		CALGB100104 ⁴	
<i>Follow up</i>	60.1 months		30 months		45 months		34 months	
<i>Median age</i>	70years		71years		55years		59 years	
	VMP	MP	MPR-R + MPR	MP	R	Placebo	R	Placebo
	n=327	n=328	n=305	n=154	n=306	n=302	n=231	n=229
<u>HAEMAT SPM</u>	3 (0.9%)	3(0.9%)	12(3.9%)	1(0.6%)	13(4.2%)	5(1.6%)	8(3.4%)	1(0.4%)
<u>SOLID SPM</u>	16(4.8%)	10(3%)	9(2.9%)	3(1.9%)	10(3.2%)	4(1.3%)	10(4.3%)	5(2.1%)
<u>TOTAL</u>	19	13	21	4	23	9	18	6

VMP, Bortezomib-Melphalan-Prednisone; MP, Melphalan-Prednisone; MPR-R, Melphalan-Prednisone-Lenalidomide followed by Lenalidomide; R, Lenalidomide; SPM, Second Primary Malignancy; AML, Acute myeloblastic leukemia; MDS, Myelodysplastic syndrome

Incidence of Second Primary Malignancies in Normal Population



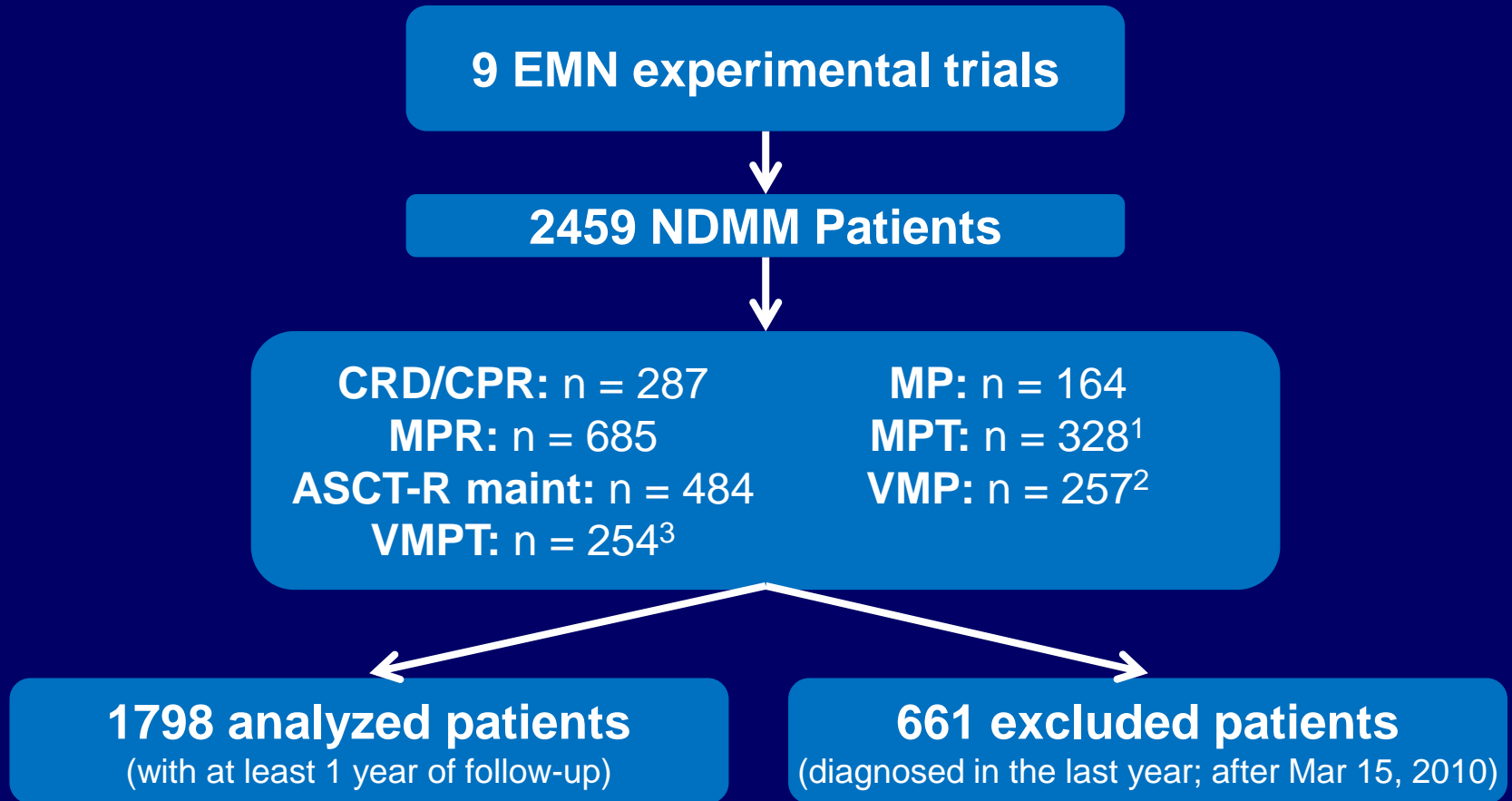
CALGB 100104: Cumulative Incidence Risk of SPM, PD, Death Updated



CALGB 100104 IMW 2013
follow up to January 7, 2013

The cumulative incidence risk of second primary cancers was greater in the **lenalidomide** group ($p=0.034$). The cumulative incidence risks of progressive disease ($p=0.004$) and death ($p<0.001$) were greater in the **placebo** group.

Retrospective Study Design

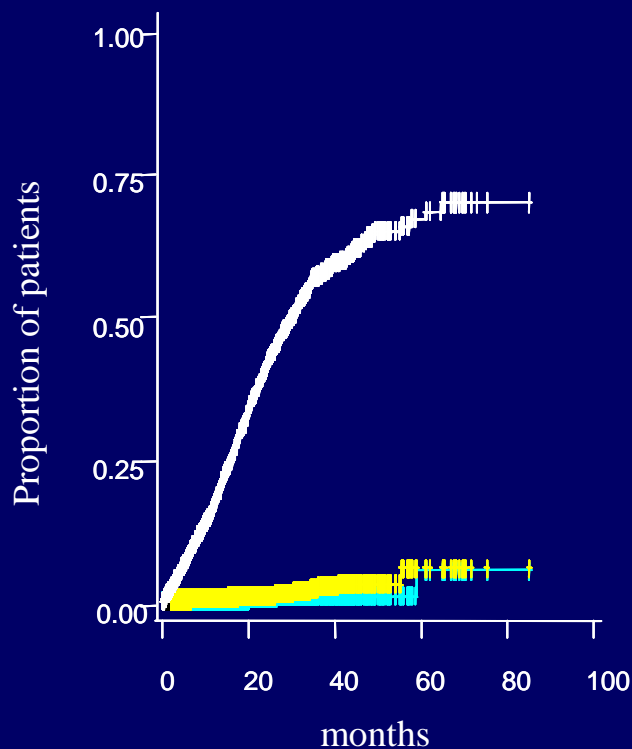


ASCT-R, autologous stem cell transplantation followed by lenalidomide maintenance; CRD, cyclophosphamide, lenalidomide, dexamethasone; CPR, cyclophosphamide, prednisone, lenalidomide; EMN, European Myeloma Network; MP, melphalan, prednisone; MPR, melphalan, prednisone, lenalidomide; MPT, melphalan, prednisone, thalidomide; NDMM, newly diagnosed multiple myeloma; SPM, second primary malignancy; VMP, bortezomib, melphalan prednisone; VMPT, bortezomib, melphalan, prednisone, thalidomide.

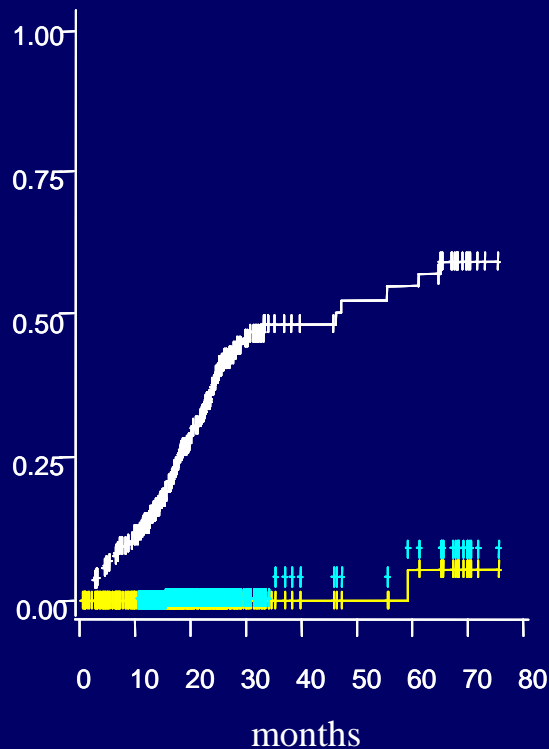
1. Palumbo A, et al. *Blood*. 2008;112:3107-3114.
 2. Palumbo A, et al. *J Clin Oncol*. 2010;28:5101-5109.
- Gay F, et al. *Eur J Haematol*. 2010;85:200-208.
www.clinicaltrials.gov.

Second Primary Malignancies and MM Progression Risk

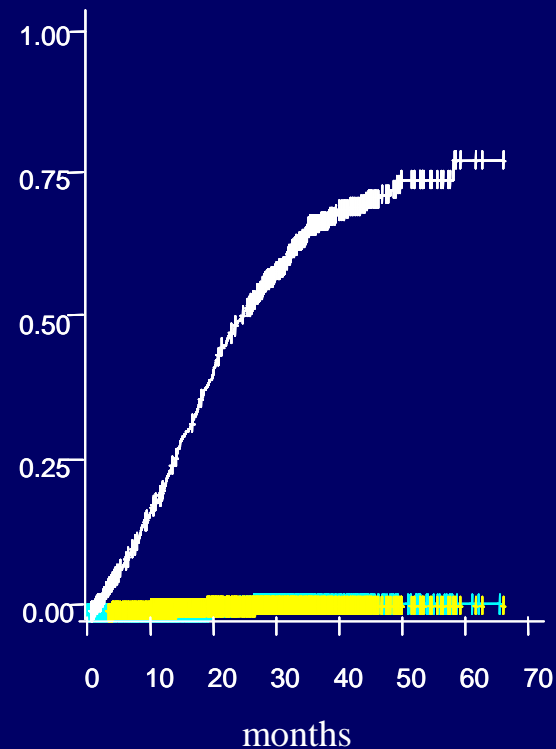
All patients



Lenalidomide

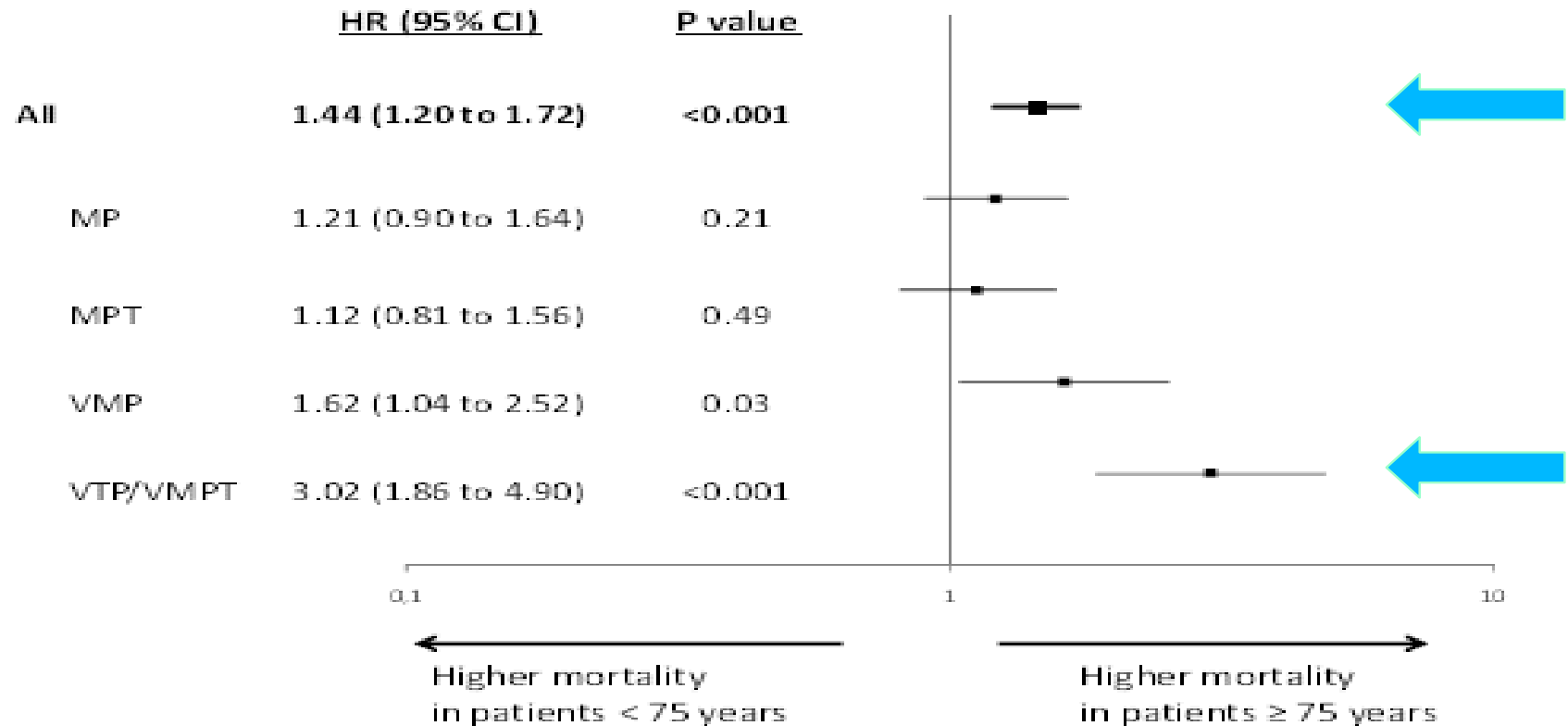


No Lenalidomide



— Progression or death — Solid SPMs — Hematologic SPMs

L'età è un fattore negativo sulla sopravvivenza dei pazienti di nuova diagnosi affetti da MM

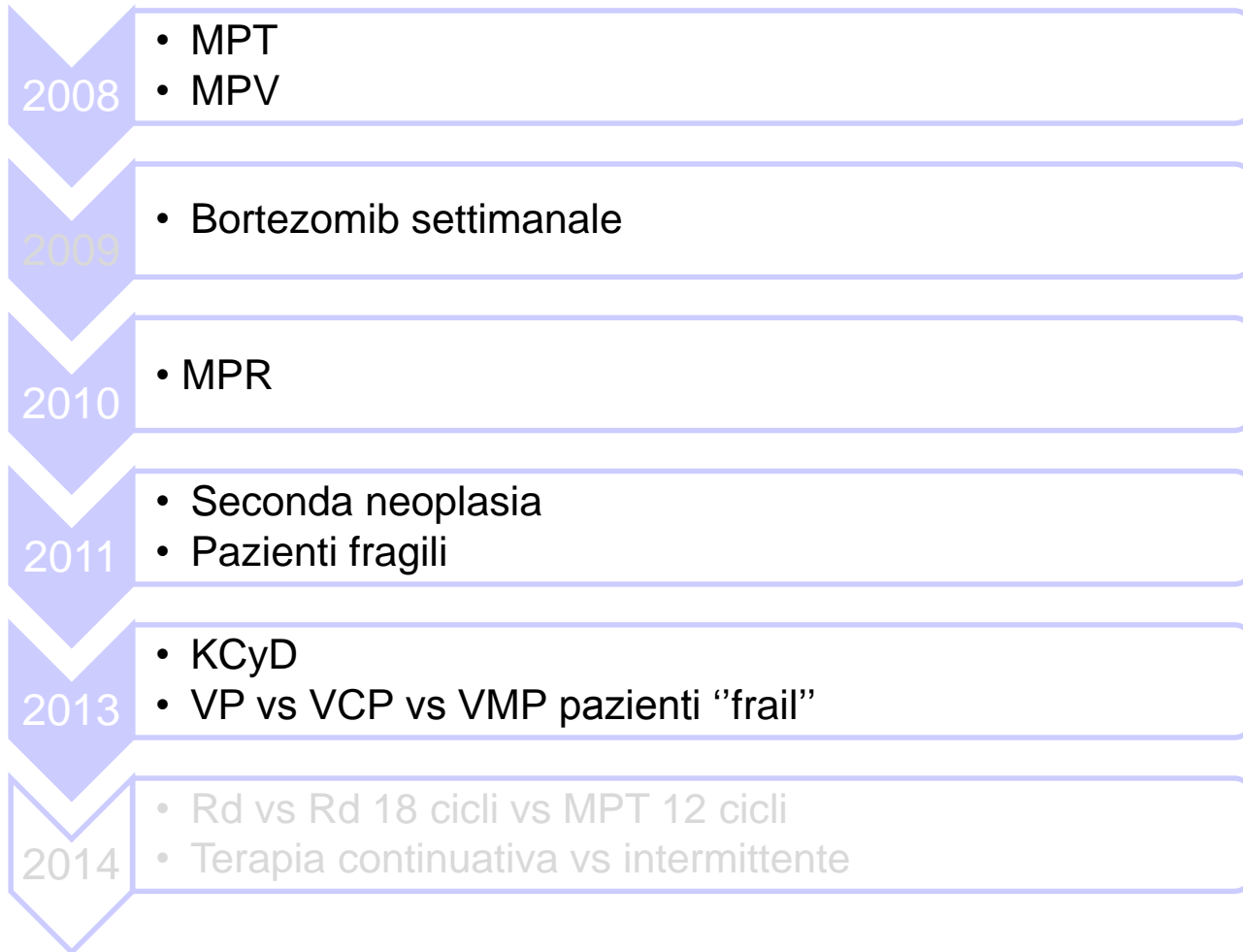


New treatment algorithm for elderly MM

PATIENT STATUS ASSESSMENT		
- Age		
- ADL		
- IADL		
- Charlson co-morbidity score		
FIT	UNFIT	FRAIL
Age <80 yr	Fit >80 yr	Unfit >80 yr
ADL 6	ADL 5	ADL ≤4
IADL 8	IADL 6-7	IADL ≤5
Charlson 0	Charlson 1	Charlson ≥2
Go-go	moderate-go	slow-go
Full-dose regimens Dose level 0	Reduced-dose regimens Dose level -1	Reduced-dose Palliative approach Dose level -2

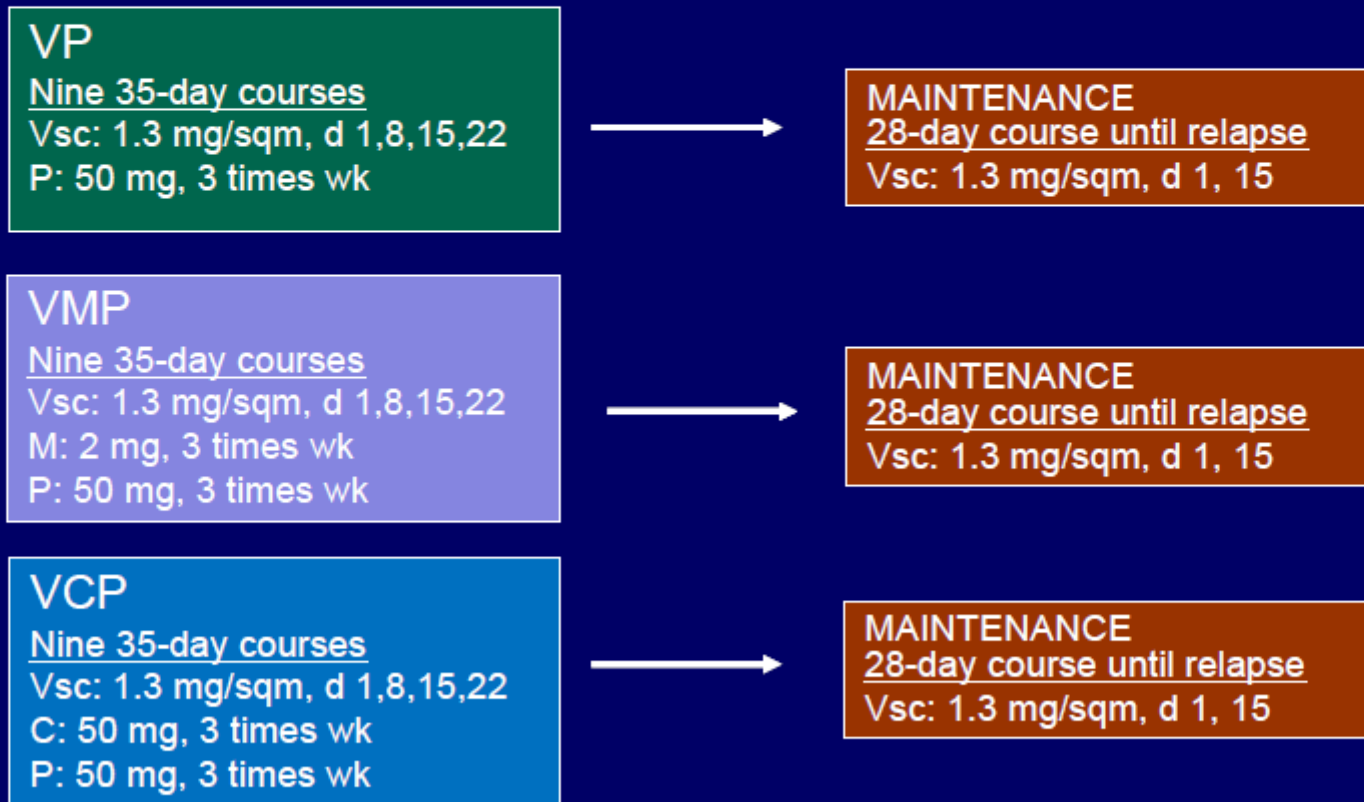
ADL, Activity of Daily Living; IADL, Instrumental Activity of Daily Living; ASCT, autologous stem cell transplantation

pazienti non eleggibili per il trapianto

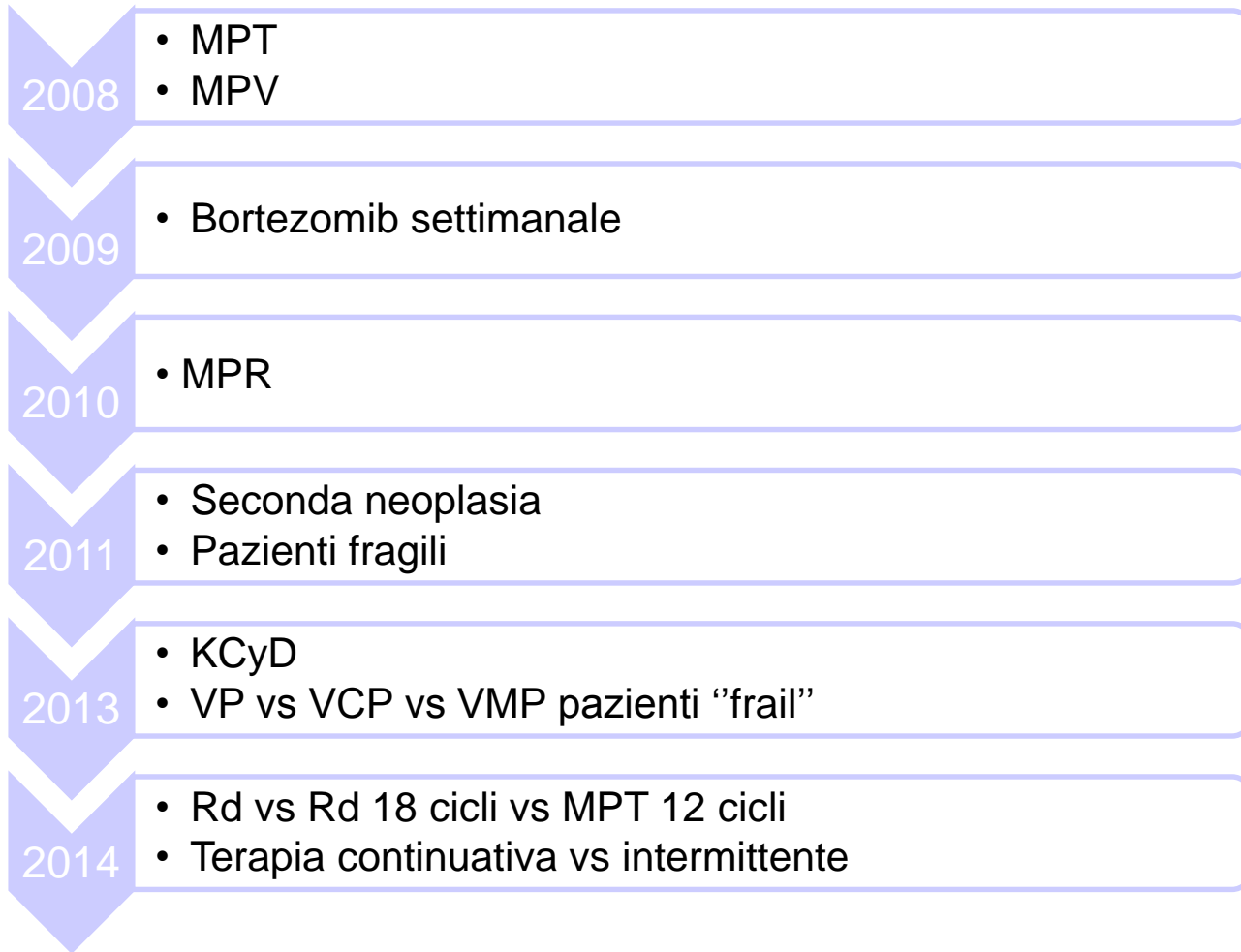


Treatment schema

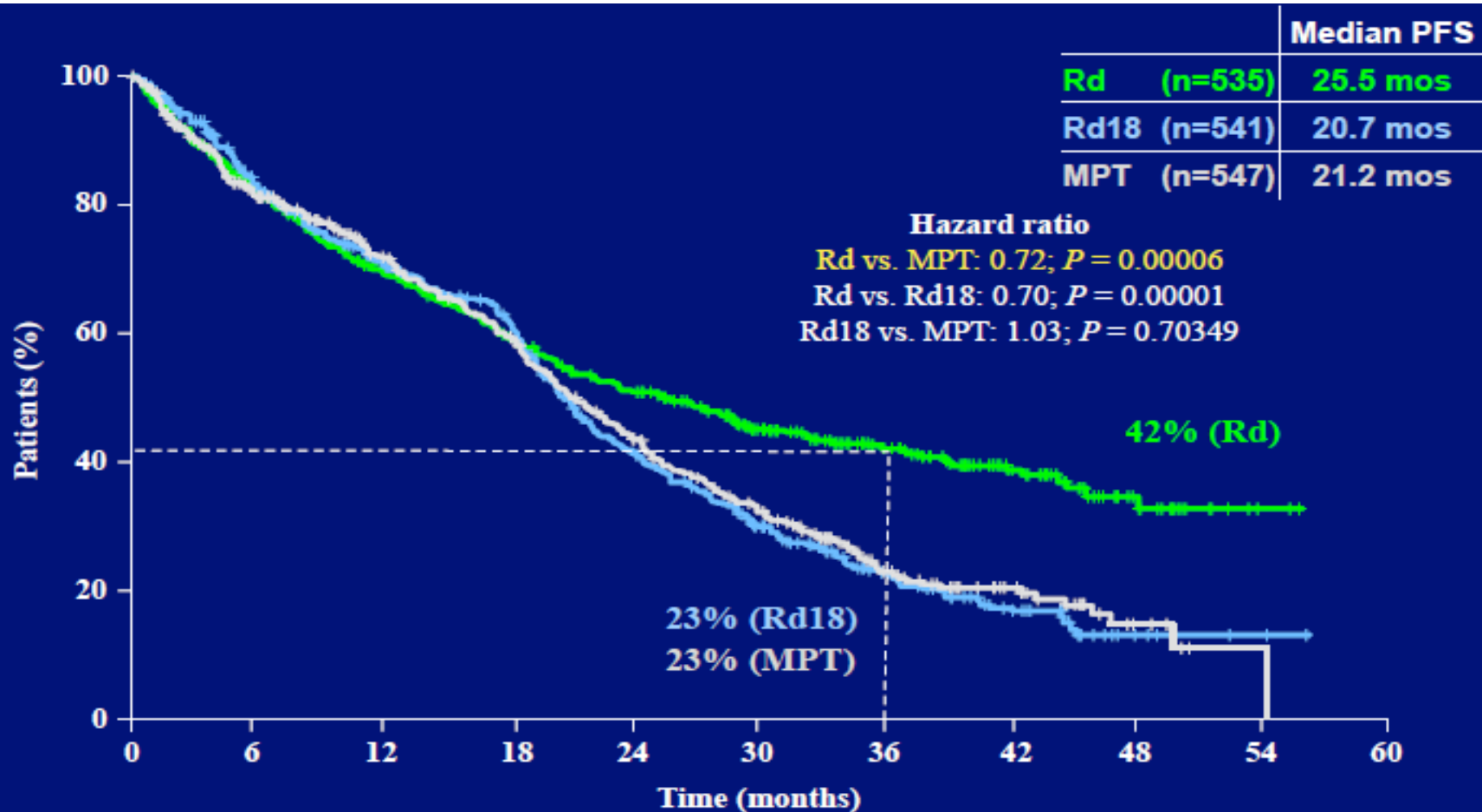
- **152** patients
- **≥ 75 years** or younger with co-morbidities
- At baseline: **geriatric assessment (ADL, IADL, Charlson)**



pazienti non eleggibili per il trapianto



FIRST: Progression-free Survival



	0	6	12	18	24	30	36	42	48	54	60
Rd	535	400	319	265	218	168	105	55	19	2	0
Rd18	541	391	319	265	167	108	56	30	7	2	0
MPT	547	380	304	244	170	116	58	28	6	1	0

Trattamenti di Induzione

Terapia durata definita

~~MPT~~

~~(Melfalan, Prednisone, Talidomide)~~

~~approvato per pazienti di nuova diagnosi
non elegibili per le alte dosi di
chemioterapia~~

~~età ≥ 65 anni~~

~~Marzo 2009~~

MPV

(Melfalan, Prednisone, Velcade)

approvato per pazienti di nuova
diagnosi non elegibili per le alte dosi
di chemioterapia

età ≥ 65 anni

Luglio 2009

Terapia continuativa

Rd

Lenalidomide, Desametasone

approvato per pazienti di nuova diagnosi
non elegibili per le alte dosi di
chemioterapia

Possibile strategia terapeutica

Progressione



Terapia A



Terapia B

Esempio: VMP

Fixed duration treatment

Progressione



Terapia A

Terapia B

Esempio: RD

Continuous treatment

pazienti eleggibili al trapianto

Terapia di induzione
consolidamento
mantenimento

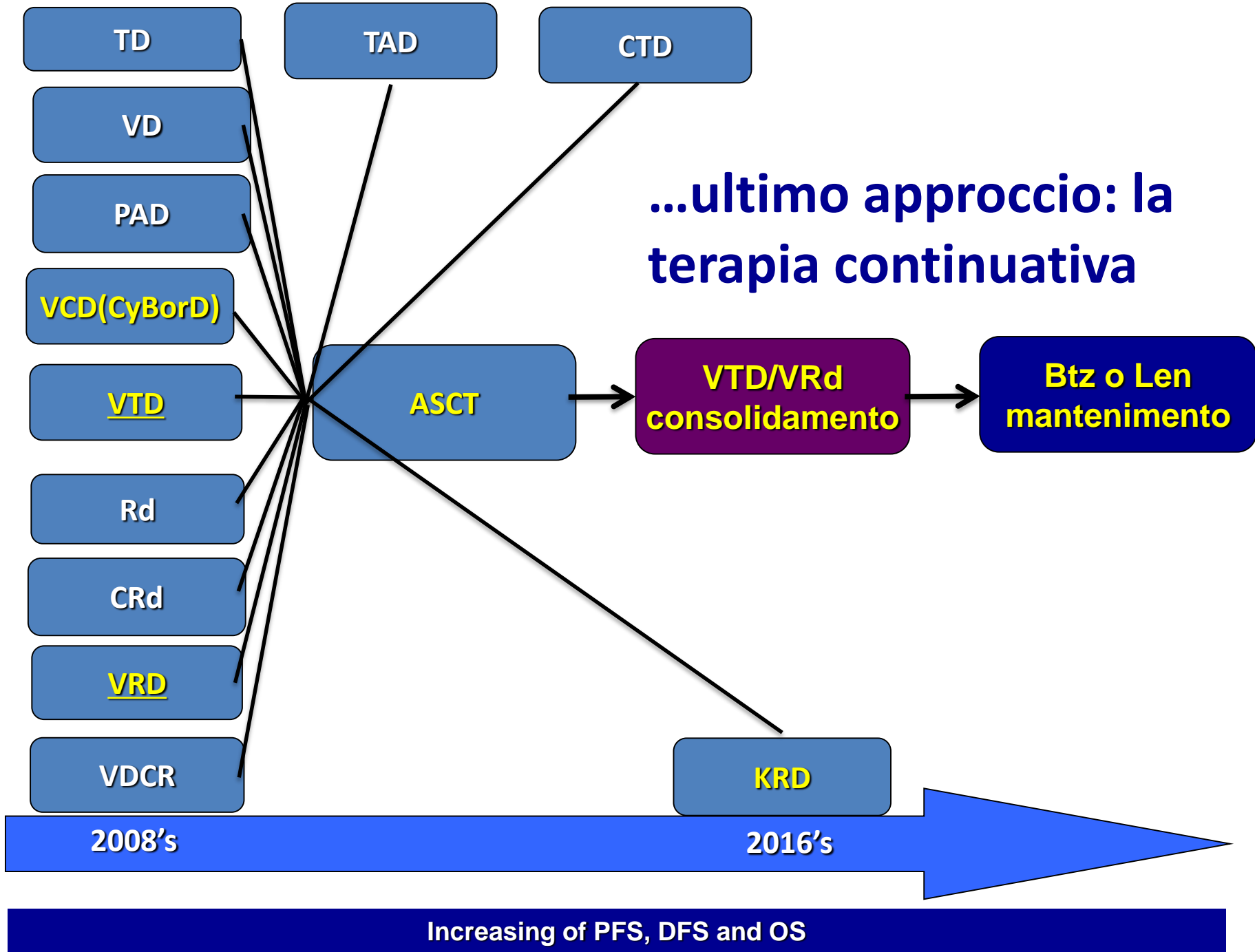
Trapianto in induzione
vs in recidiva

pazienti eleggibili al trapianto

Terapia di induzione
consolidamento
mantenimento

Trapianto in induzione
vs in recidiva

**...ultimo approccio: la
terapia continuativa**



TD

TAD

CTD

VD

PAD

VCD(CyBorD)

VTD

ASCT

VTD/VRd
consolidamento

Btz o Len
mantenimento

Rd

CRd

VRD

VDCR

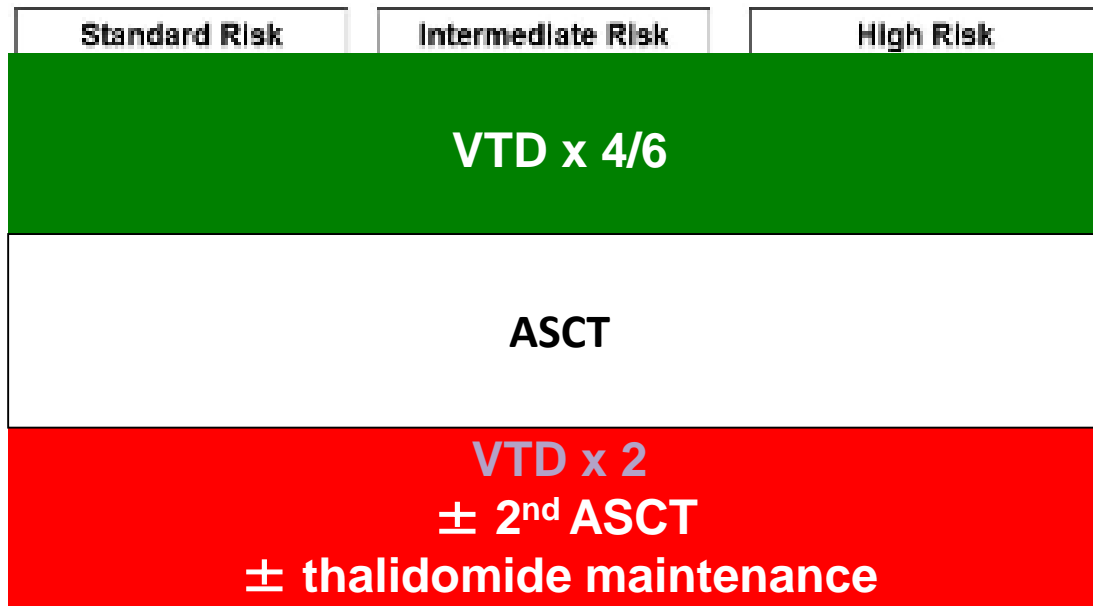
KRD

2008's

2016's

Increasing of PFS, DFS and OS

Approccio terapeutico nei pazienti elegibili al trapianto “The Italian Real Life”



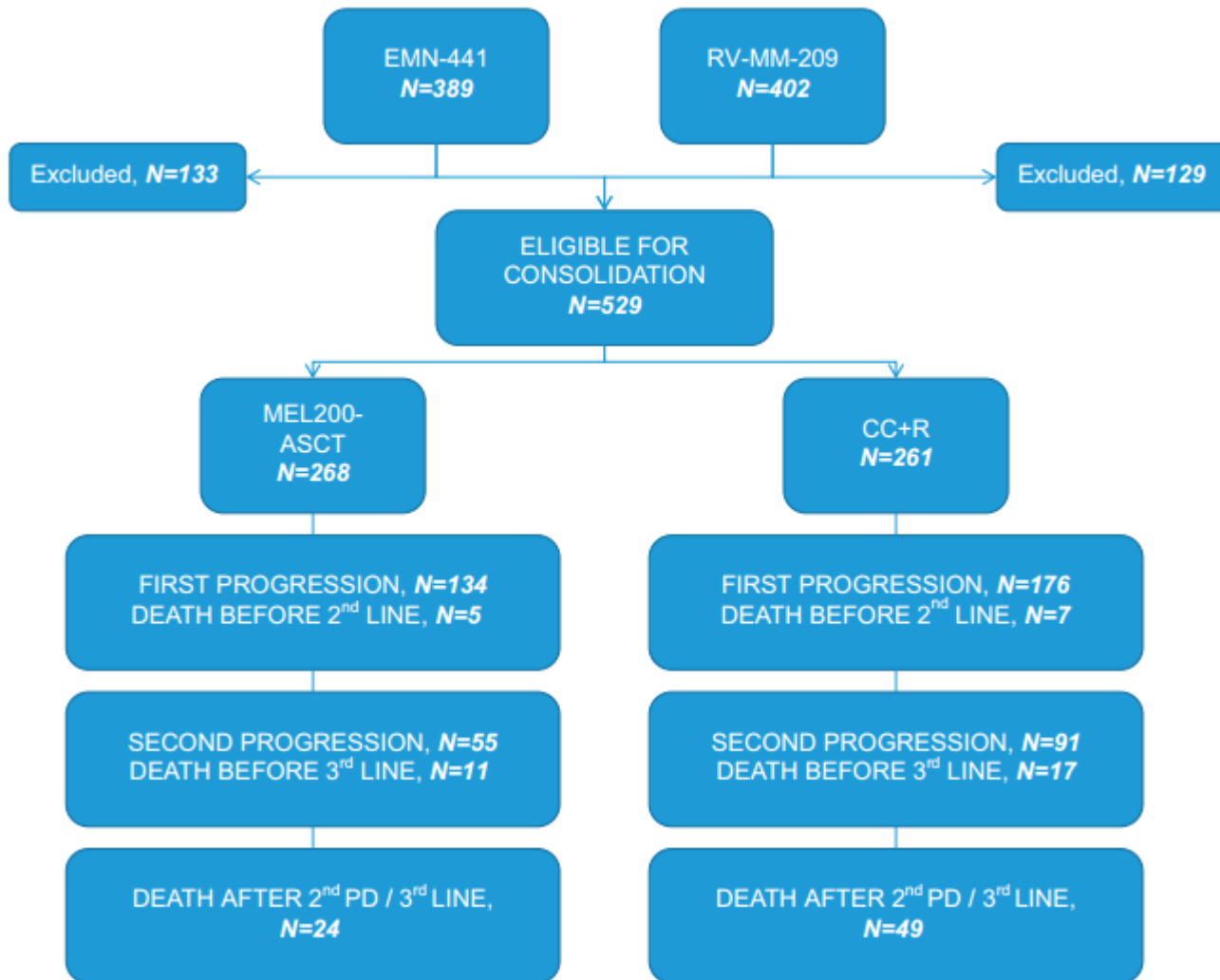
2017: EMA approva Lenalidomide in mantenimento

pazienti eleggibili al trapianto

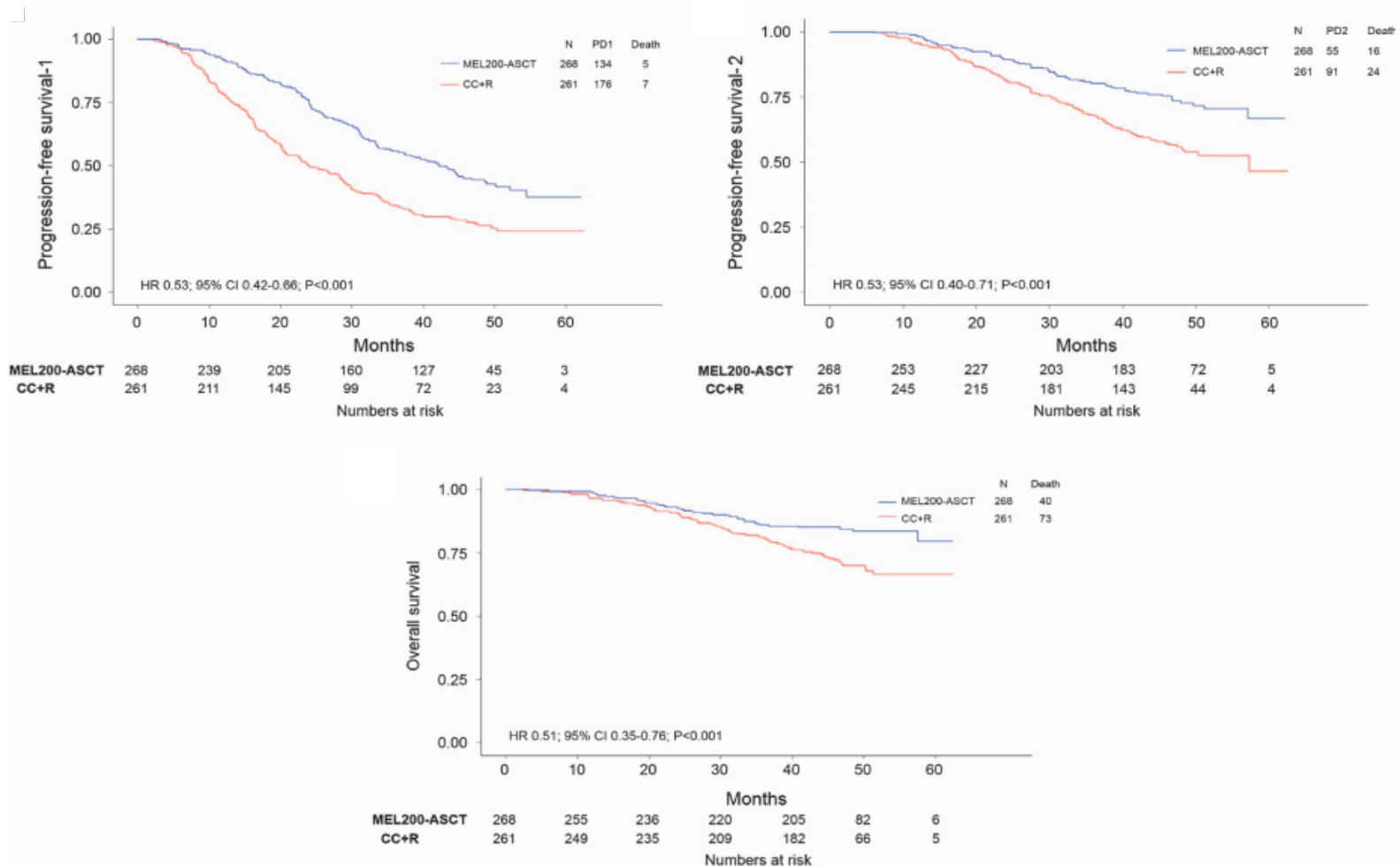
Terapia di induzione
consolidamento
mantenimento

Trapianto in induzione
vs in recidiva

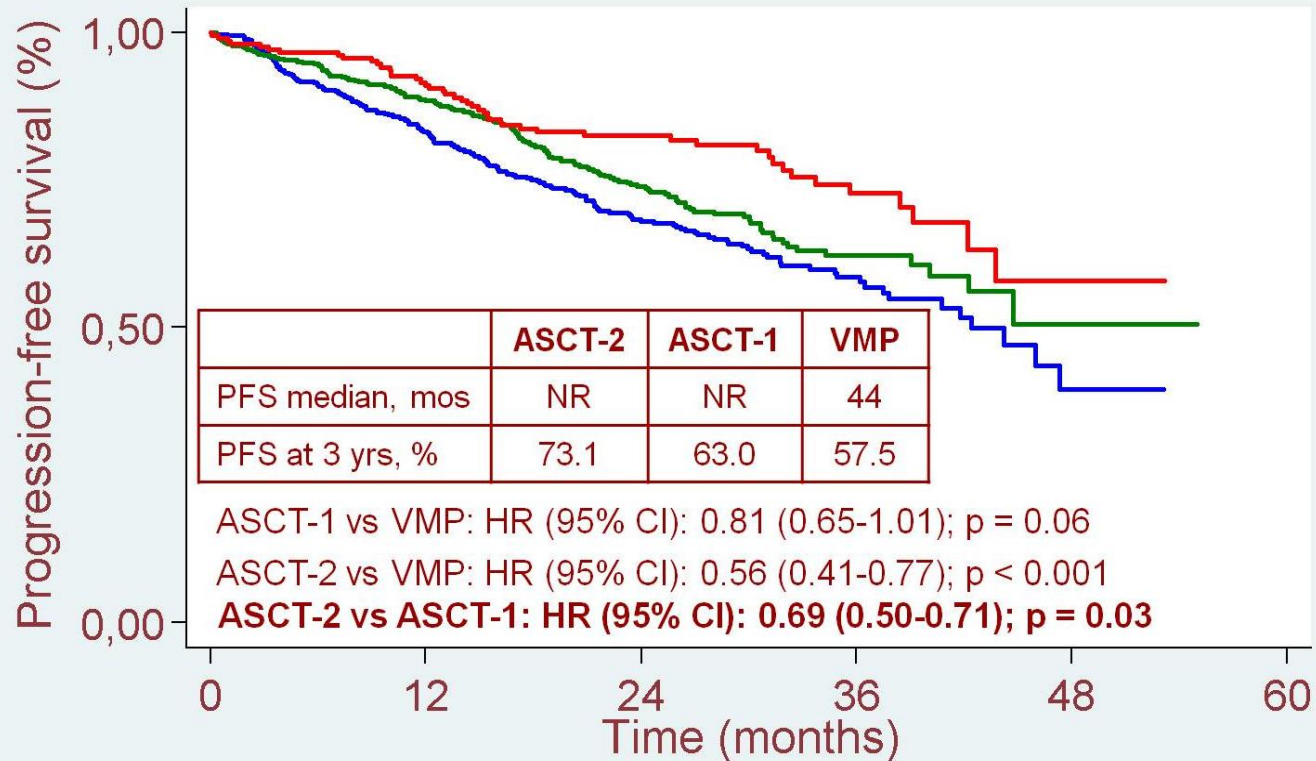
Autologous transplant vs oral chemotherapy and lenalidomide in newly diagnosed young myeloma patients: a pooled analysis



Autologous transplant vs oral chemotherapy and lenalidomide in newly diagnosed young myeloma patients: a pooled analysis



PFS: protocollo EMN02/HO95

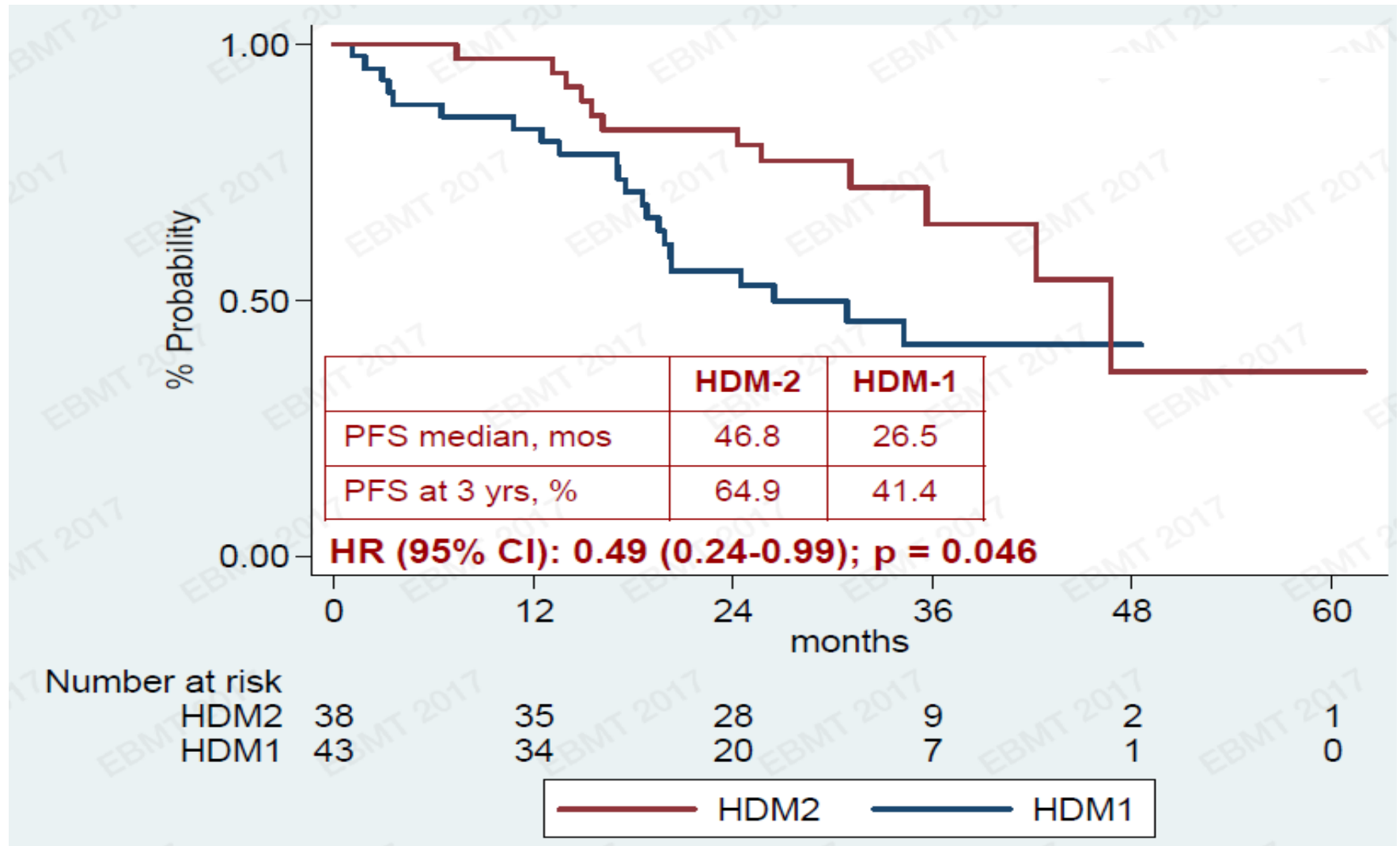


Number at risk

ASCT-2	207	179	119	44	3	0
ASCT-1	488	391	230	64	2	0
VMP	497	383	230	74	10	0

— VMP — ASCT-1 — ASCT-2

PFS: alto rischio citogenetico

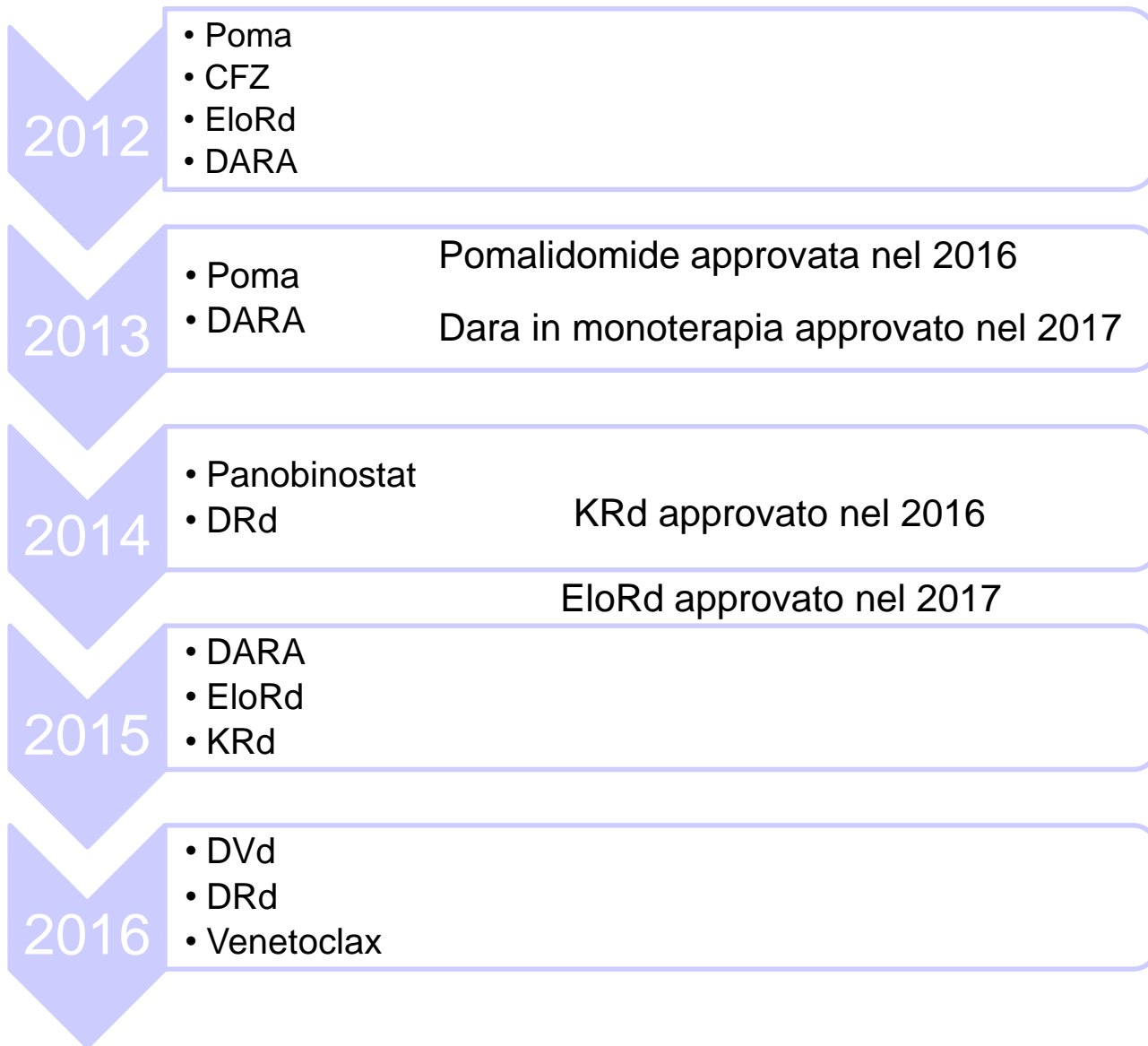


Risultati dell'autotrapianto nel MM induzione con i nuovi farmaci

- Risposte complessive **70 - 100 %**
- **Risposte complete** **31 - 57 %**
- Sopravvivenza mediana **3 anni** **>85%**
- **PFS 3 anni** **>65%**
- Mortalità correlata a trapianto **< 2 %**
- Buona qualità di vita post auto

Indicazione assoluta nei pazienti < 65/70 aa

pazienti in recidiva/refrattari



2017

- Federico Silvestri Udine
- Tolomeo Anna Vercelli
- Ursoleo Paola Milano
- Garvey Kimberly Ancona
- Tomassetti Simona Rimini
- Ferrara Maria Giovanna Napoli
- Fani Arianna Firenze
- Veltroni Marinella Firenze
- Camera Andrea Caserta
- Califano Catello Pagani
- Attingenti Enrico Caserta
- Maesano Silvana Sondrio

Domande

- Citogenetica/citofluorometria
 - Eseguita in alcuni centri ma non per indirizzo terapeutico
 - Terapia Anziano
 - MPT 1 centro
 - VMP o Rd decisione sulla base delle caratteristiche del paziente, malattia e logistica
 - Terapia Giovane
 - VTD 4icli + Auto + e VDT no Tal 2 centri Lena
 - NON SEMPRE DOPPIO TRAPIANTO

Recidiva

Difficoltà di eseguire KRd o EloRd (centri prescrittori)

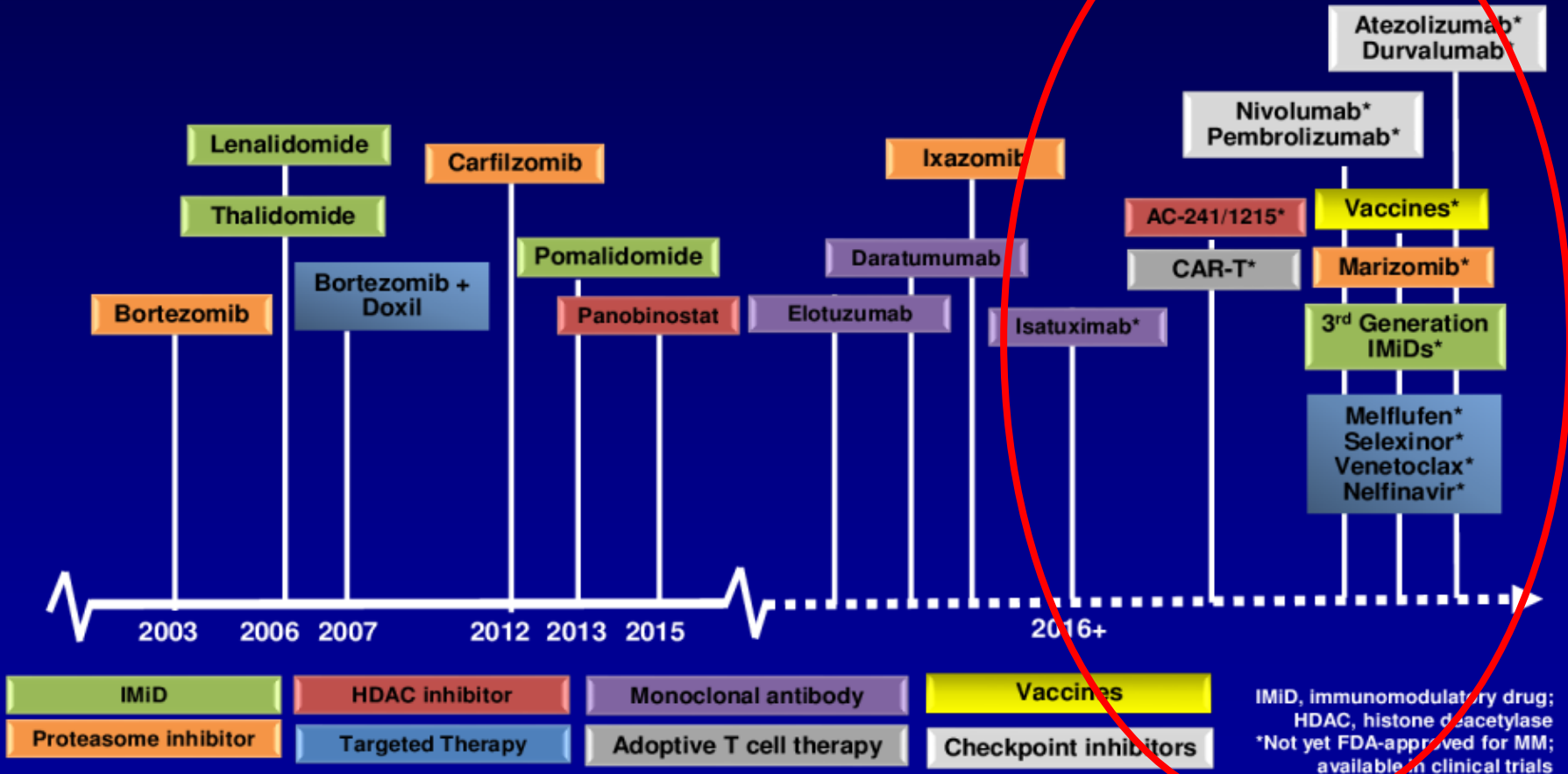
Secondo autotrapianto considerato se almeno
24 mesi

Daratumumab difficoltà organizzative

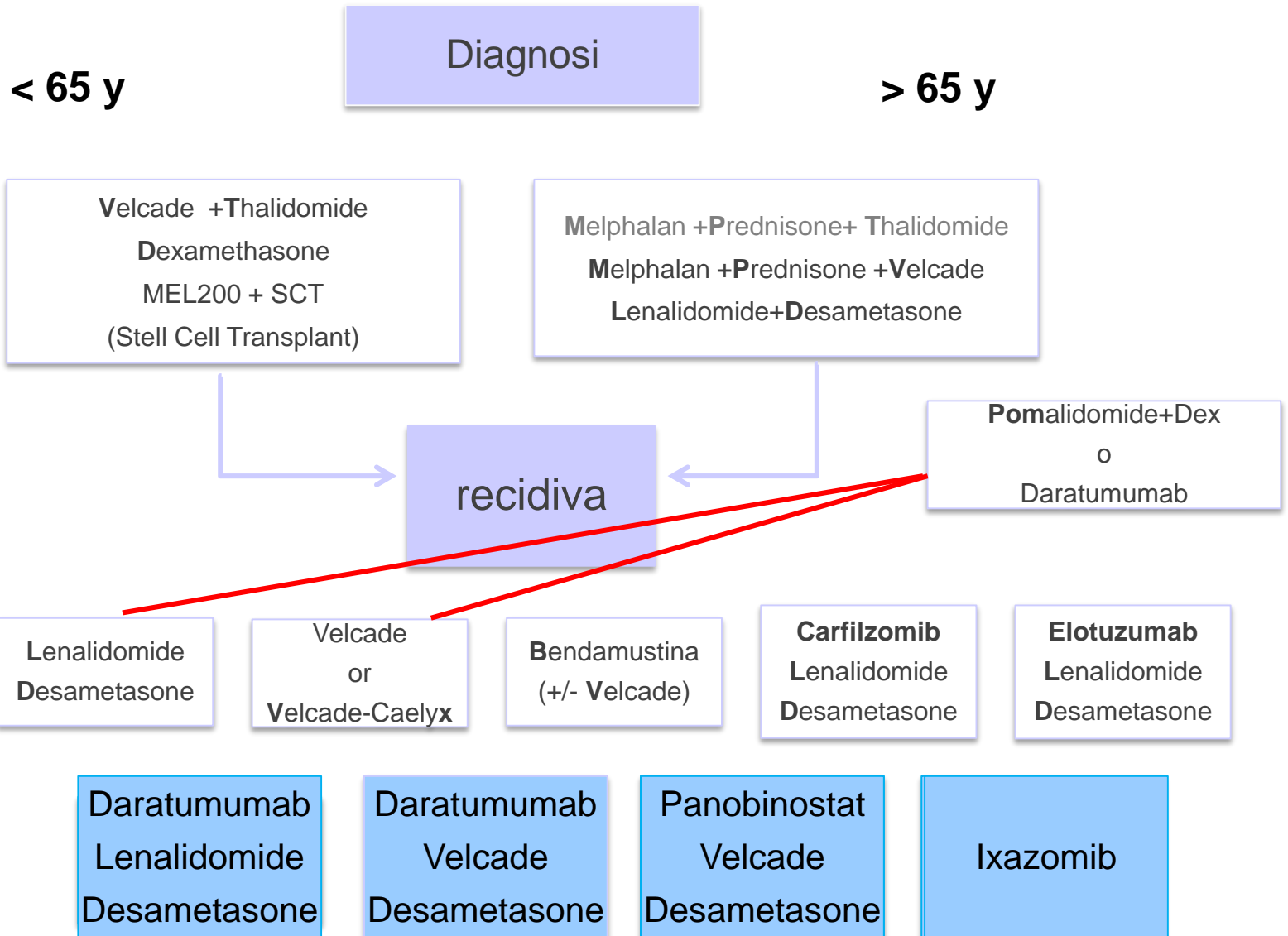
Continuing Evolution of Multiple Myeloma Treatment: Selected New Classes and Targets 2016- 2017

1st Generation Novel Agents

2nd Generation Novel Therapies/ Immunotherapy



Algoritmo terapeutico



Grazie!!