

# Highlights from IMS 20th meeting 2023

**Monica Galli**

**L'evoluzione della terapia  
di mantenimento: con  
due o con tre farmaci?**

30-31 gennaio 2024

BOLOGNA, Royal Hotel Carlton

# Disclosures of Monica Galli

Company name	Research support	Employee	Consultant	Stockholder	Speakers bureau	Advisory board	Other
Amgen			X			X	
BMS			X			X	
GSK			X			X	
Janssen			X			X	
Menarini						X	
Sanofi			X			X	
Takeda			X			X	

# History of MM Maintenance: RCTs

**1975: Intermittent courses of Carmustine+Prednisone vs continuous courses of Melphalan+Prednisone vs no chemotherapy -> NO difference**

**1986-2006: Glucocorticosteroids/Dexamethasone -> increase in PFS**

**1998-2004: Interferon -> not consistent increase in PFS**

**2006-2012: Post-ASCT Thalidomide -> increase in PFS **AIFA approved since 2009****

**2012->: Post-ASCT Lenalidomide -> increase in PFS & OS **AIFA approved since 2018****

**2012: Post-ASCT Bortezomib -> increase in PFS & OS**

# Newer Drugs for Post-ASCT Maintenance

**Single agent:**

**Daratumumab (CASSIOPEIA)**

**Ixazomib (TOURMALINE-3)**

**Belantamab Mafodotin (DREAMM-9)**

**Iberdomide (EMN26)**

**Carfilzomib (CARDAMON)**

**Isatuximab (RADAR: standard risk arm)**

# Maintenance: post-ASCT only?

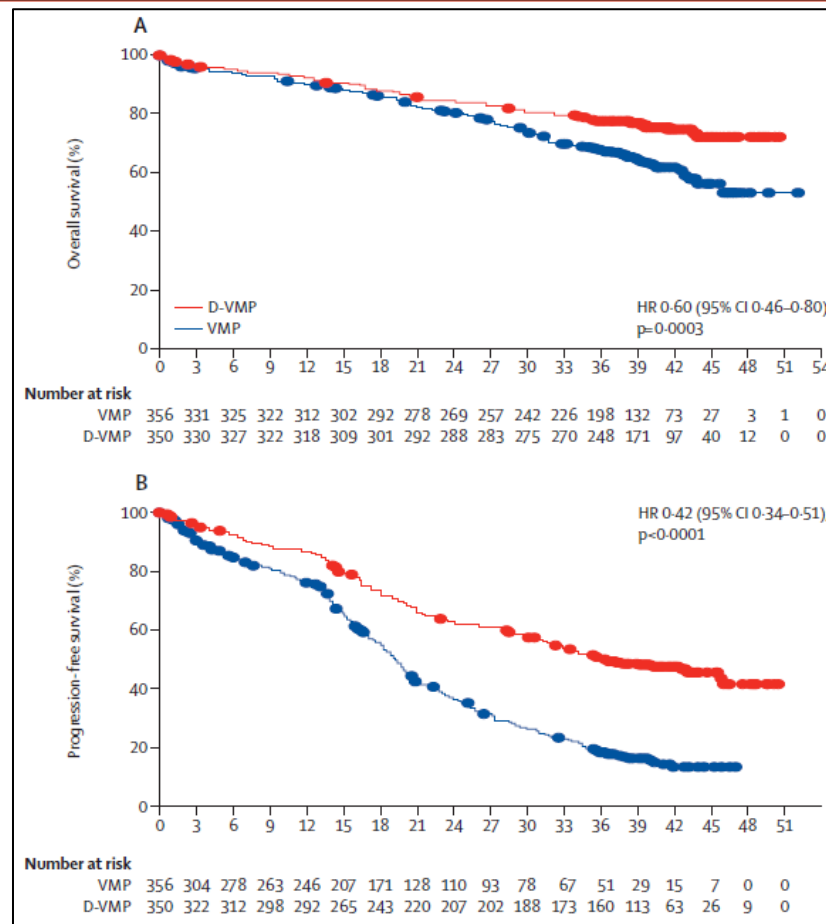
# ALCYONE Clinical Trial: OS & PFS

Dara-VMPx9 followed by Dara maintenance

VS  
VMPx9

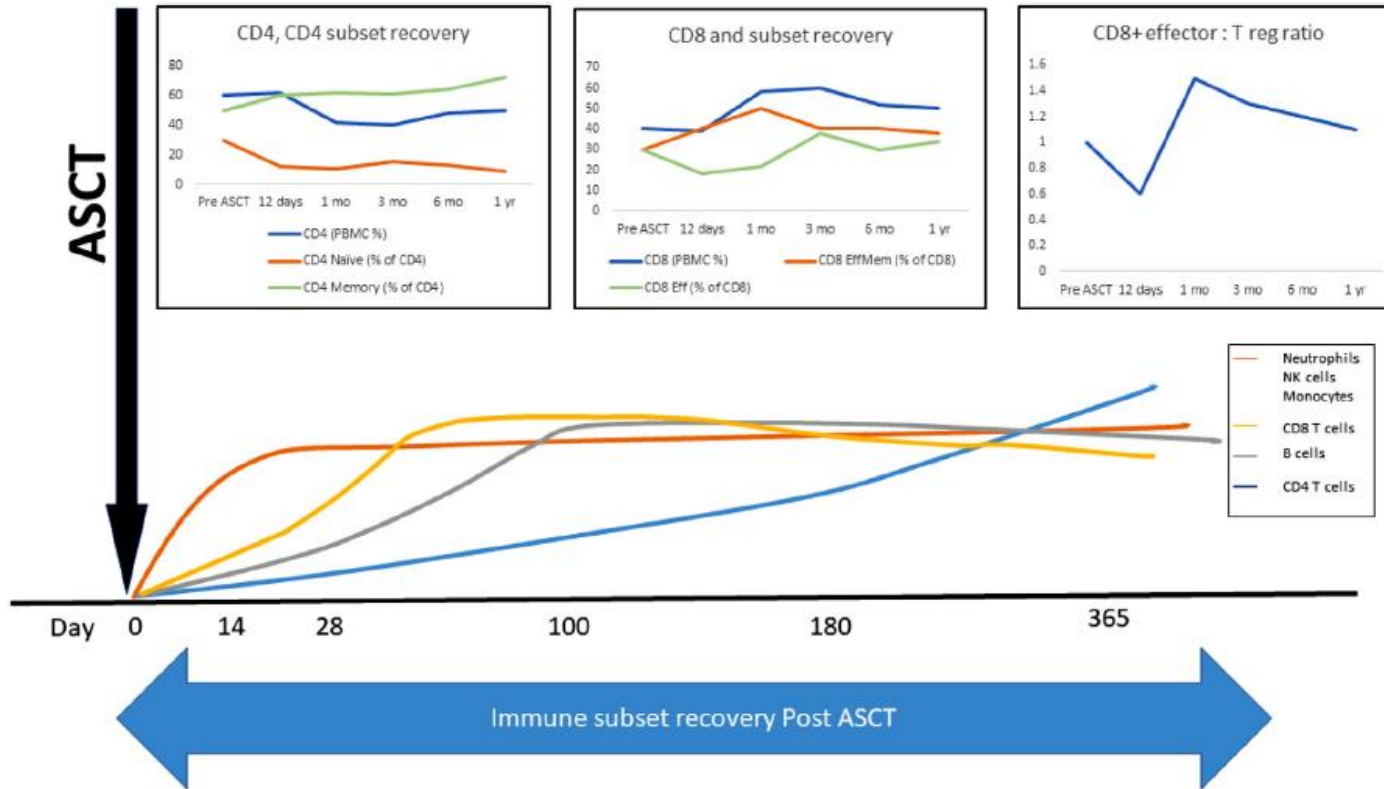
Daratumumab induction & maintenance  
significantly improve:

- 3 yr OS rate, **78.0** vs **67.9%**
- mPFS, **36.4** vs **19.3** months



# **Maintenance: why is it useful particularly in the post-ASCT setting?**

# Immune Reconstitution post-ASCT



**Better T-reg/T-eff Ratio**

**Early NK cells recovery**

**Higher tumor-specific T cells**



**Maintenance: better with 2 or 3 drugs?**

# Newer Drugs for MM Maintenance

Two drugs:

**Lenalidomide/Dexamethasone (IMROZ, EMN-20)**

**Daratumumab/Lenalidomide (PERSEUS, DraMMatic, AURIGA, EQUATE, GRIFFIN, GEM2017FIT)**

**Daratumumab/Ixazomib (EMN-18)**

**Isatuximab/Lenalidomide (GMMG-HD7, RADAR)**

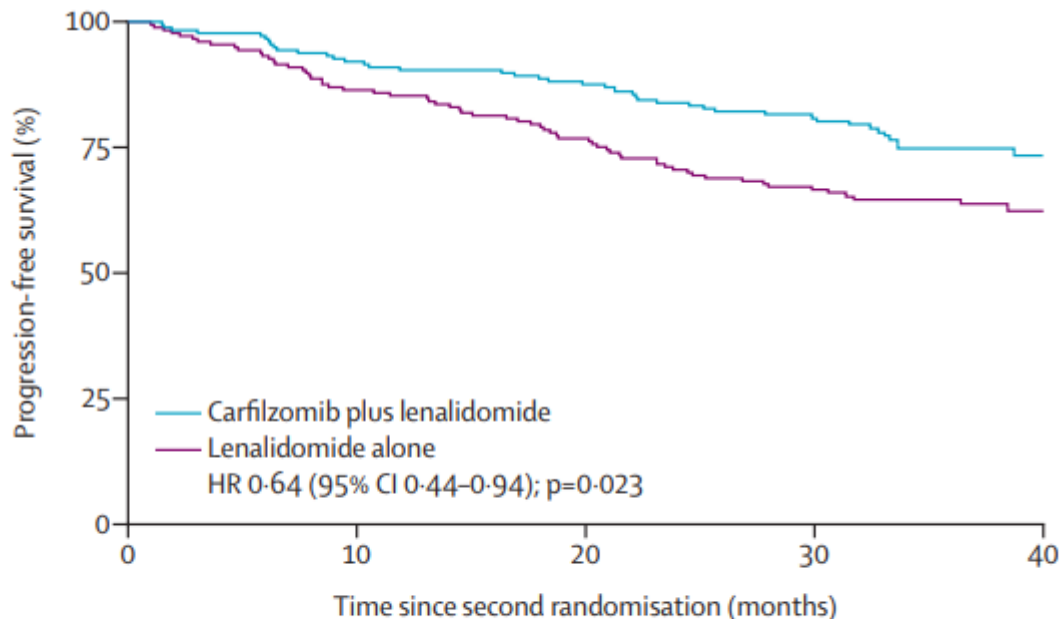
**Carfilzomib/Lenalidomide (FORTE)**

**Ixazomib/Lenalidomide (Myeloma XIV)**

**Selinexor/Lenalidomide (SeaLAND)**

**Lenalidomide/Vorinostat (NCT00729118) (only 16 pts, 2 median PLoT)**

## 2 yrs Maintenance with **KR** vs **R** in FORTE Trial: PFS



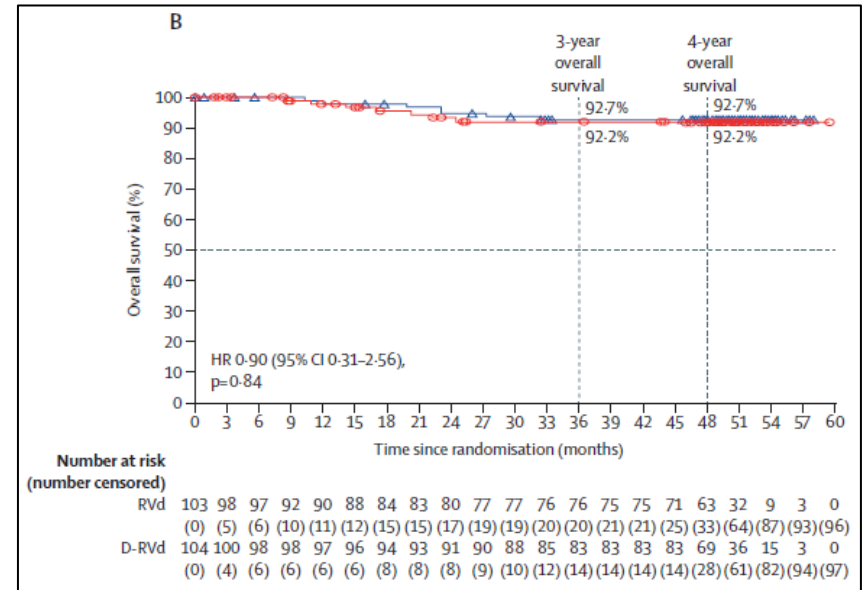
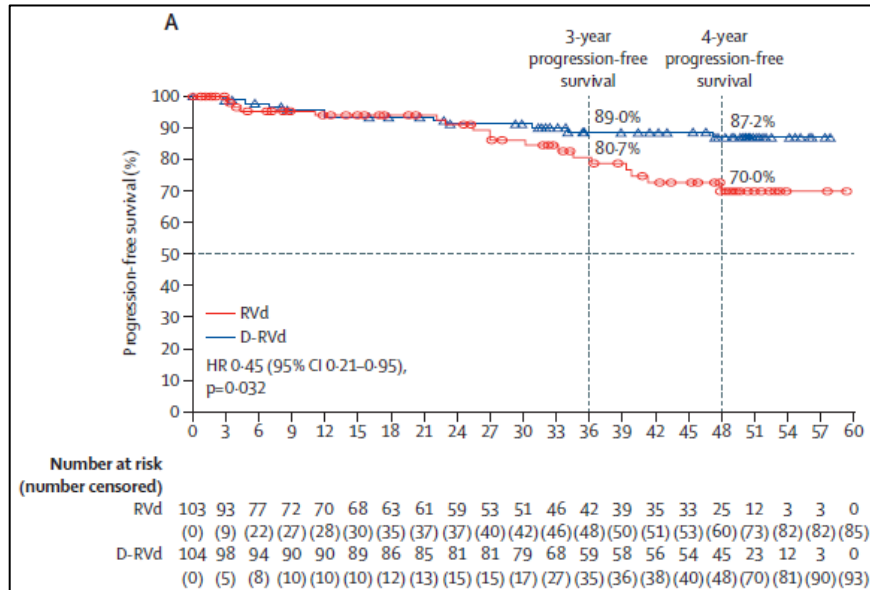
	Number at risk (number censored)				
Carfilzomib plus lenalidomide	178 (1)	162 (2)	151 (5)	123 (22)	41 (95)
Lenalidomide alone	178 (0)	154 (0)	135 (2)	108 (11)	39 (75)

# 2 yr Maintenance with Dara-R vs R in GRIFFIN Trial: PFS & OS by ITT

Dara-RVdx4 -> ASCT -> Dara-RVdx2 -> Dara-R maintenance

VS

RVdx4 -> ASCT -> RVdx2 -> R maintenance



# Newer Drugs for MM Maintenance

Three drugs:

Daratumumab/Lenalidomide/Dexamethasone (CEPHEUS)

Isatuximab/Lenalidomide/Dexamethasone (IMROZ)

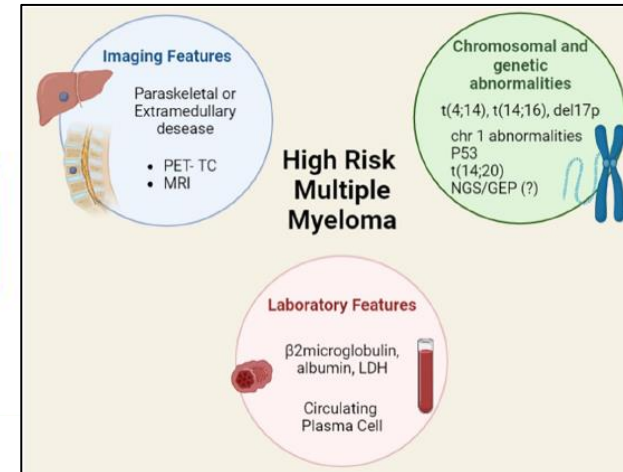
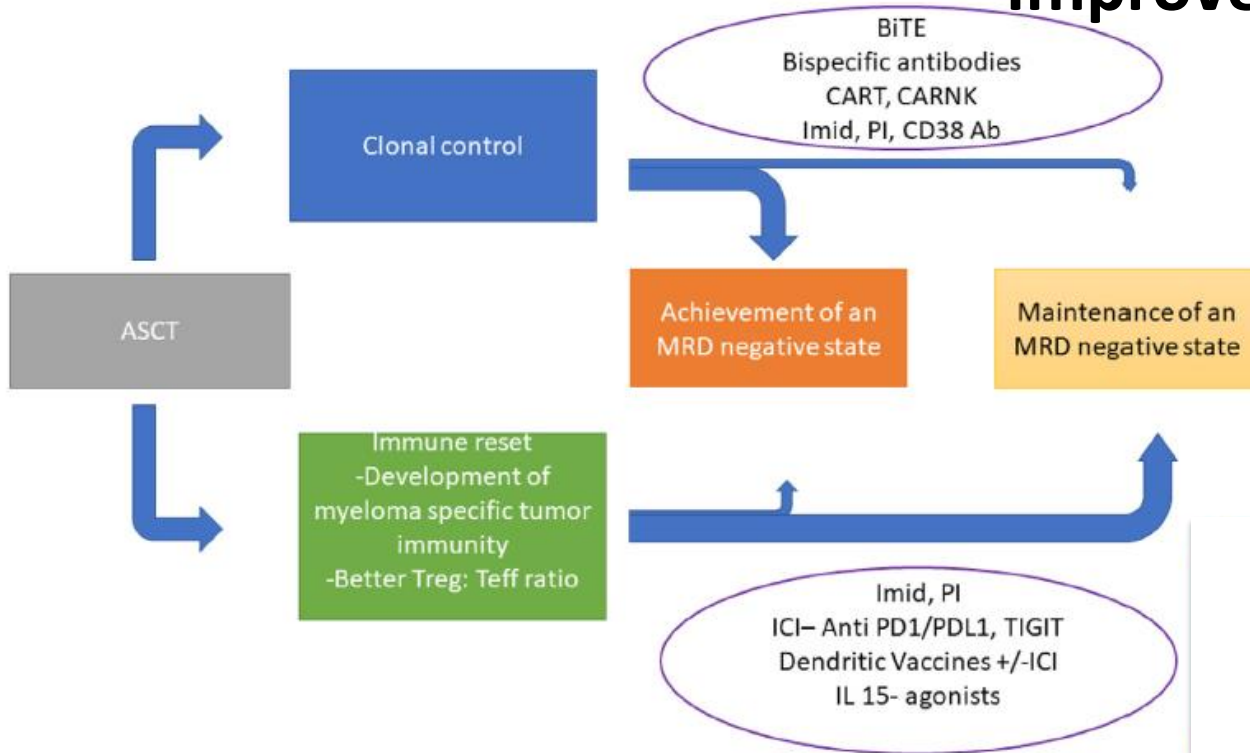
**Isatuximab/Carfilzomib/Lenalidomide (GMMG-CONCEPT)**

Carfilzomib/Lenalidomide/Dexamethasone (EMN-20; ATLAS)

Elotuzumab/Lenalidomide/Dexamethasone (NCT2495922)

Ixazomib/Lenalidomide/Dexamethasone (GEM14MAIN)

# Post-ASCT Mechanisms of Disease Control & Strategies to Improve Clinical Responses



# ATLAS: KRd vs R as post-ASCT Maintenance

**K: 20/36 mg/mq, days 1-2-8-9-15-16 on cycles 1->4; days 1-2-15-16 on cycles 5->36**

**R: 25 mg, days 1->21**

**d: 20 mg, days 1-8-15-22**

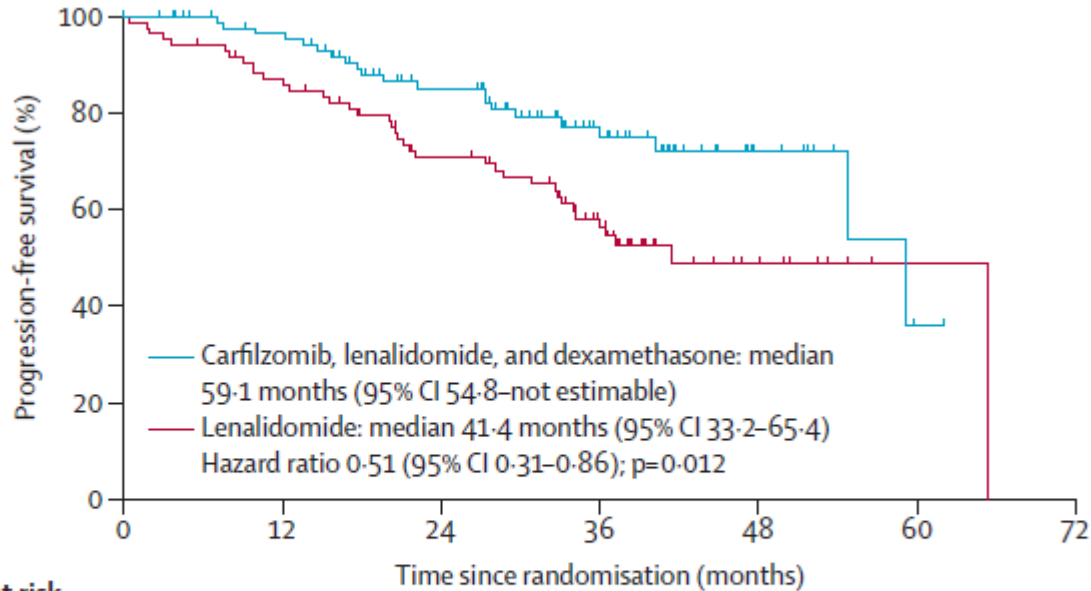
**vs**

**R: 10-15 mg, days 1->28**

**After cycle 36, all pts continued maintenance with R alone**

**Standard-risk pts who were MRD neg after cycle 6, were shifted to R alone as of cycle 9**

# ATLAS: KRd vs R as post-ASCT Maintenance



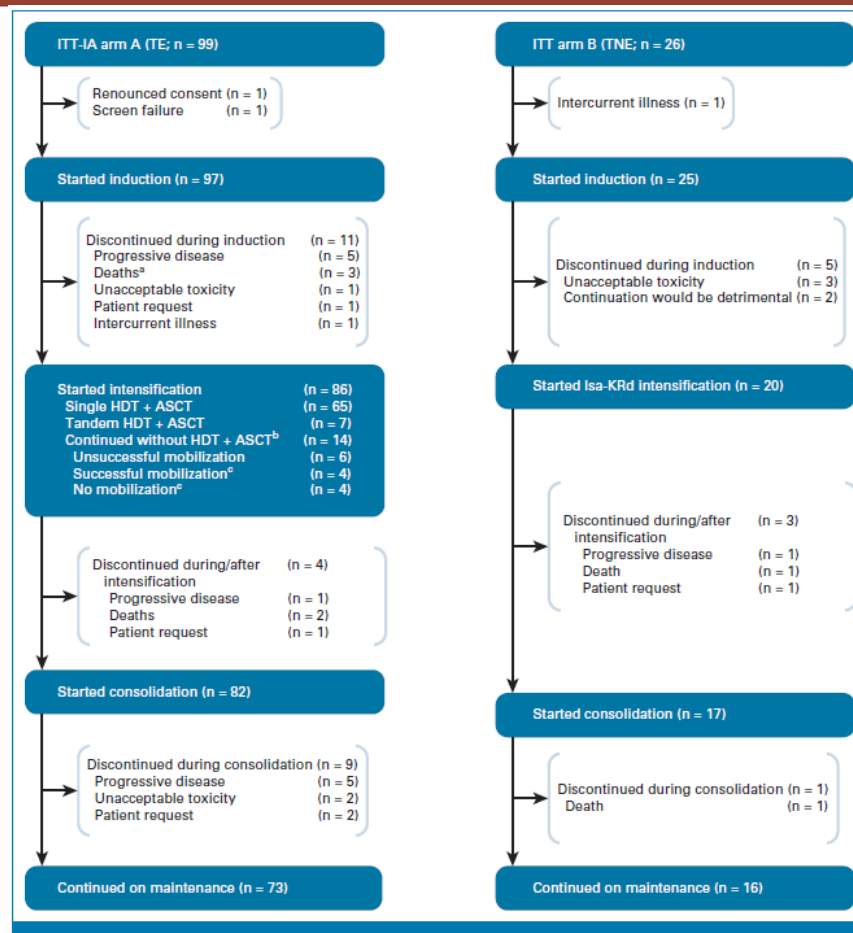
	0	12	24	36	48	60	72
<b>Number at risk (number censored)</b>							
Carfilzomib, lenalidomide, and dexamethasone	93 (0)	82 (11)	61 (20)	34 (42)	10 (62)	1 (71)	0 (72)
Lenalidomide	87 (0)	73 (3)	54 (9)	32 (21)	8 (42)	1 (48)	0 (49)



# GMMG-CONCEPT: Isa-KR (x 26 cycles) as Maintenance in TE & TNE High- Risk Pts

HR defined by ISS stage II or III combined  
with  $\geq 1$  of the following:  
del17p (in  $>10\%$  of purified cells),  
t(4;14), t(14;16),  
 $>3$  1q21 copies (amp1q21)  
primary plasma cell leukemia

Isa 10 mg/kg on days 1 & 15  
K 70 mg/sm on days 1 & 15  
R 15 mg on days 1->21



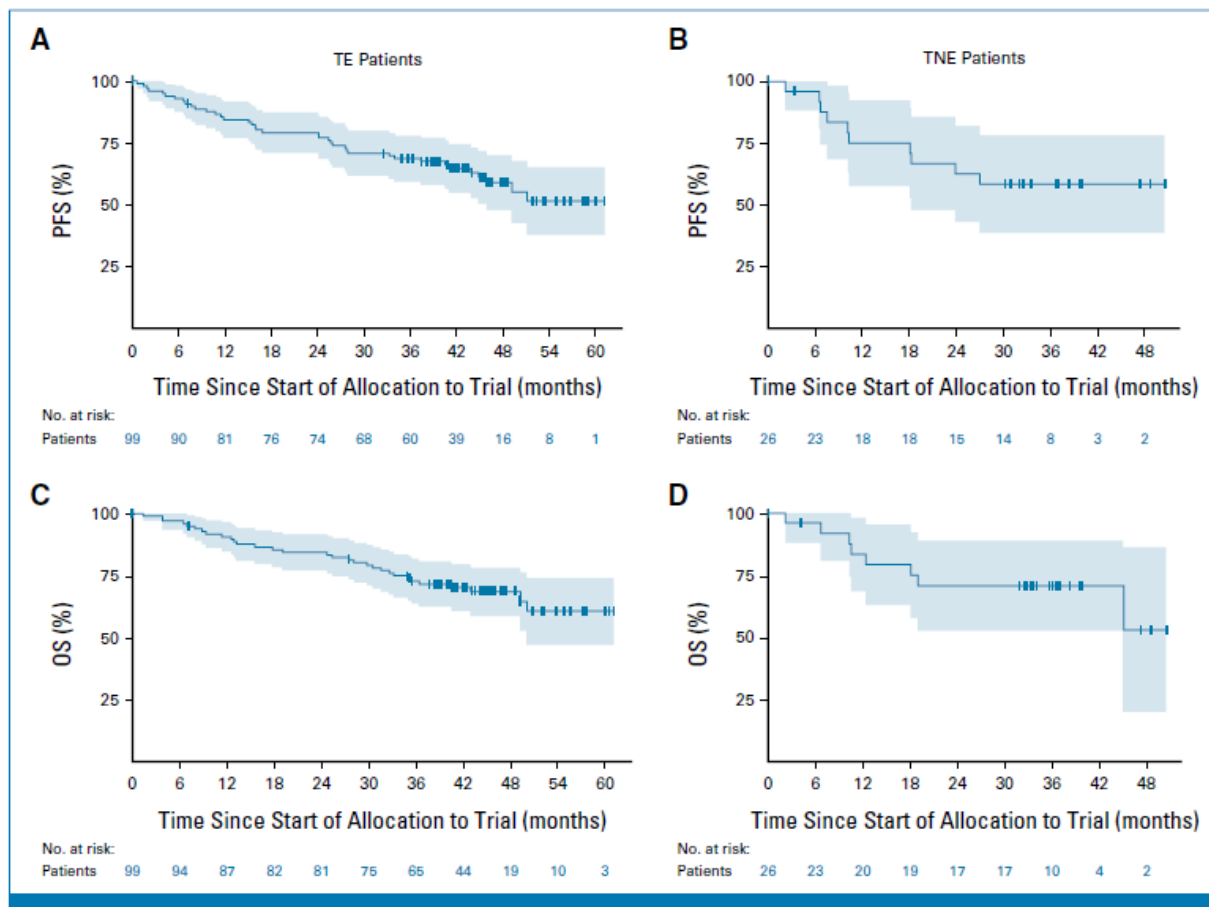
# GMMG-CONCEPT:

**PRIMARY END POINT:**

**MRD- ( $10^{-5}$ ) at the end of consolidation:**

**TE Pts: 67.7% ; TNE Pts: 54.2%**

No. (%)	TE Patients (n = 99)	TNE Patients (n = 26)
MRD negative (any time point)	81 (81.8)	18 (69.2)
Sustained MRD negativity for $\geq 6$ months	72 (72.7)	14 (53.8)
Sustained MRD negativity for $\geq 12$ months	62 (62.6)	12 (46.2)



# Conclusions

**Long-term Lenalidomide administration is SoC for post-ASCT MM maintenance**

**Bortezomib (every other week) may be considered as “off label” maintenance for post-ASCT MM with HRCA features**

**Several clinical studies are investigating the following possibilities for maintenance:**

- fixed vs long-term duration**
- combination of 2 or 3 drugs (mostly on a Lenalidomide-based backbone)**
- MRD status-driven intensity & duration**
- intensification in HR pts (for adverse CA and/or extramedullary presentation)**

# Grazie per l'attenzione

