

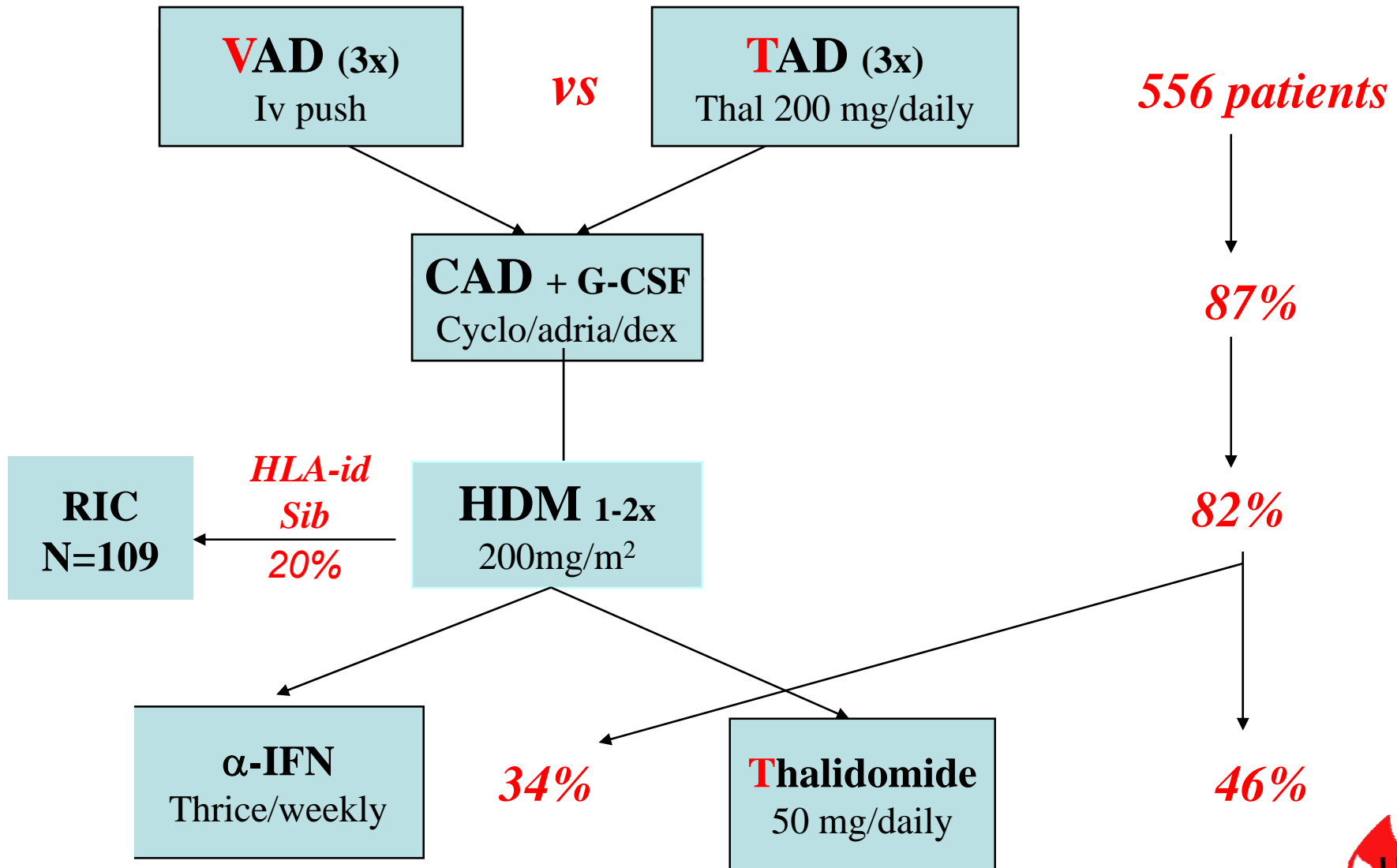


HOVON 50 MM final analysis

*A randomized phase III study on the effect of
Thalidomide combined with Adriamycin,
Dexamethasone and High Dose Melphalan in
patients with multiple myeloma*

Statistics: Bronno van der Holt

HOVON 50



Patient characteristics

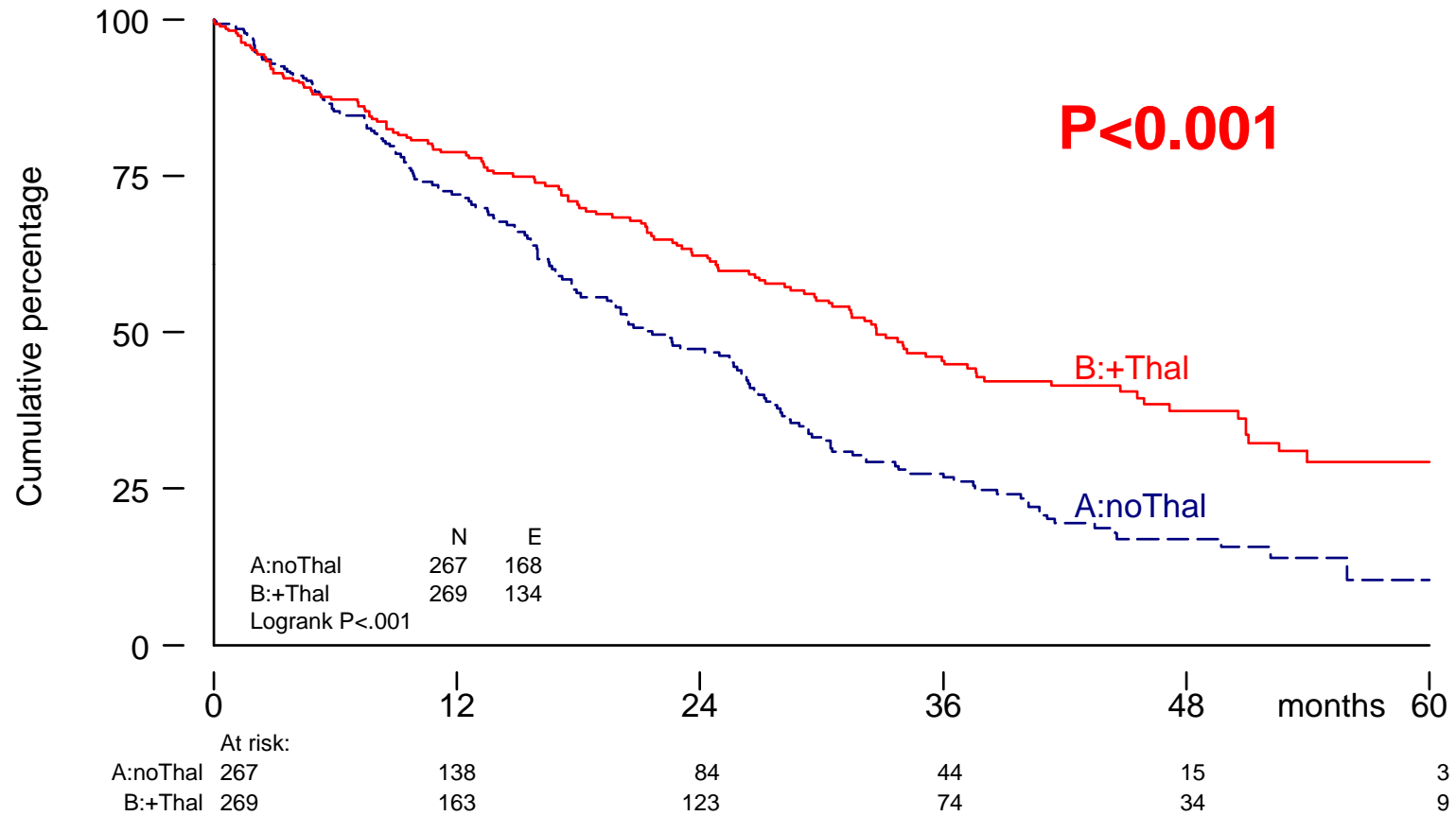
- Age median 56 years (32-65)
- Male/female 60/40
- Salmon&Durie II/III 20/80
- ISS
 - I 52%
 - II/III 48%

Equally divided in both arms

Best response on protocol

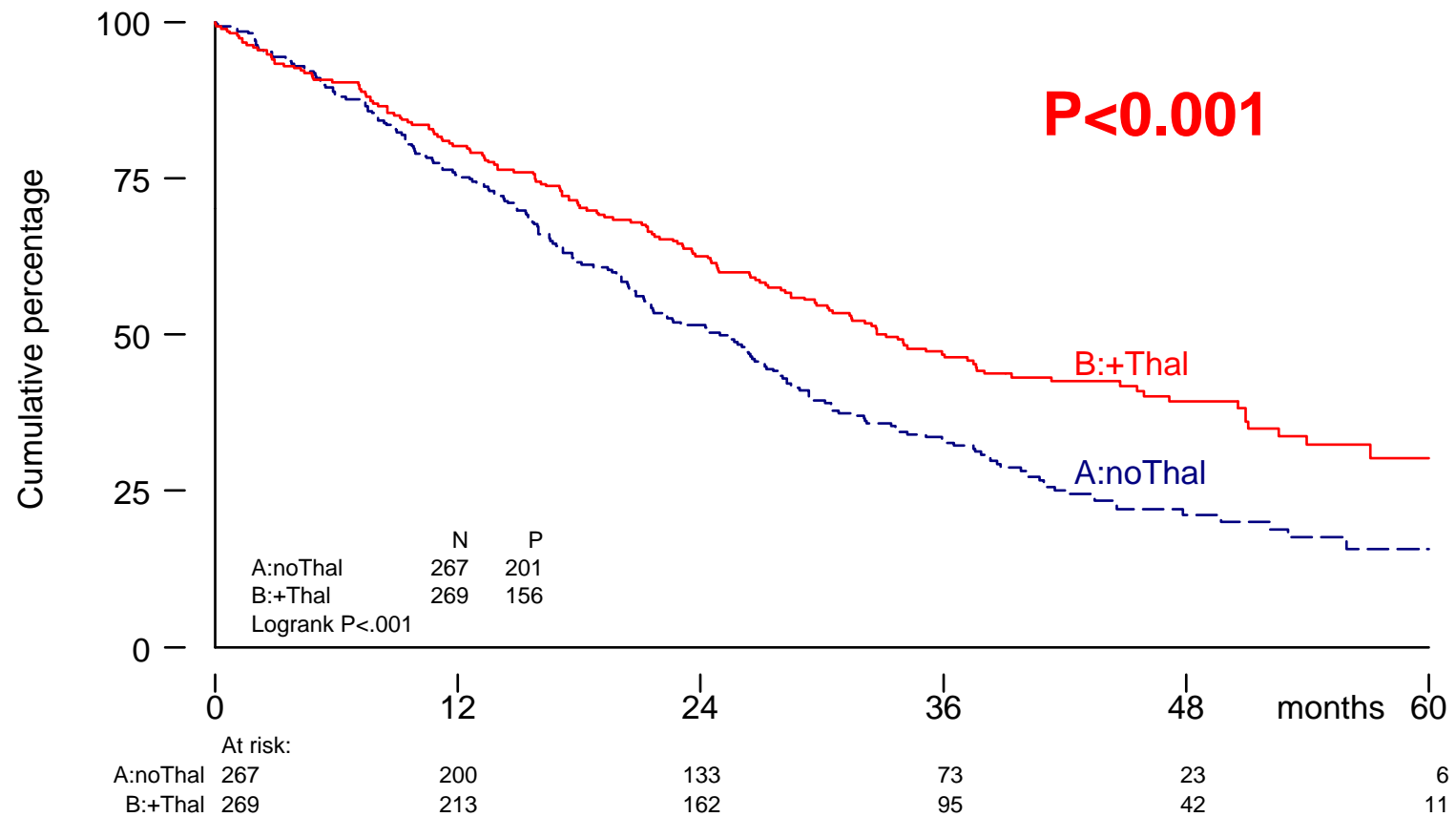
	A (VAD)	B (TAD)	p.
<u>At least</u>			
PR	79 %	87%	<0.01
VGPR	54 %	65%	<0.01
CR	21 %	30%	0.03

Event Free Survival

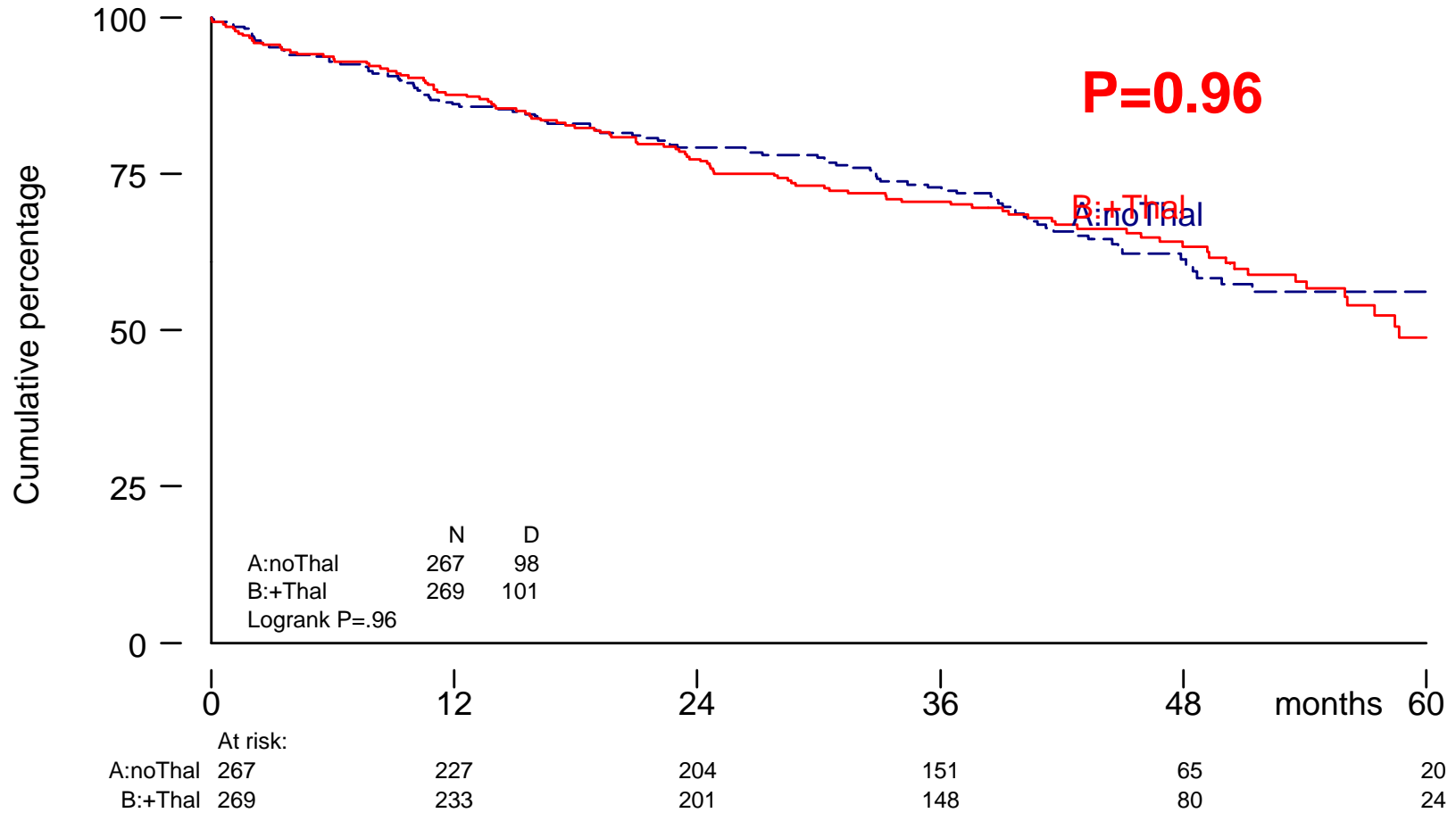


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Progression Free Survival



Survival



Thalidomide and IFN compliance

- **Induction**

- Thalidomide full dose 58%
- Thalidomide modified 13%
- **Thalidomide stopped 29%**

- **Maintenance started**

- **IFN 43%** **Thal: 67%**

- **Maintenance continued**

- IFN**

- 12 months 23%
- 24 months 15%
- 36 months 11%

- Thal**

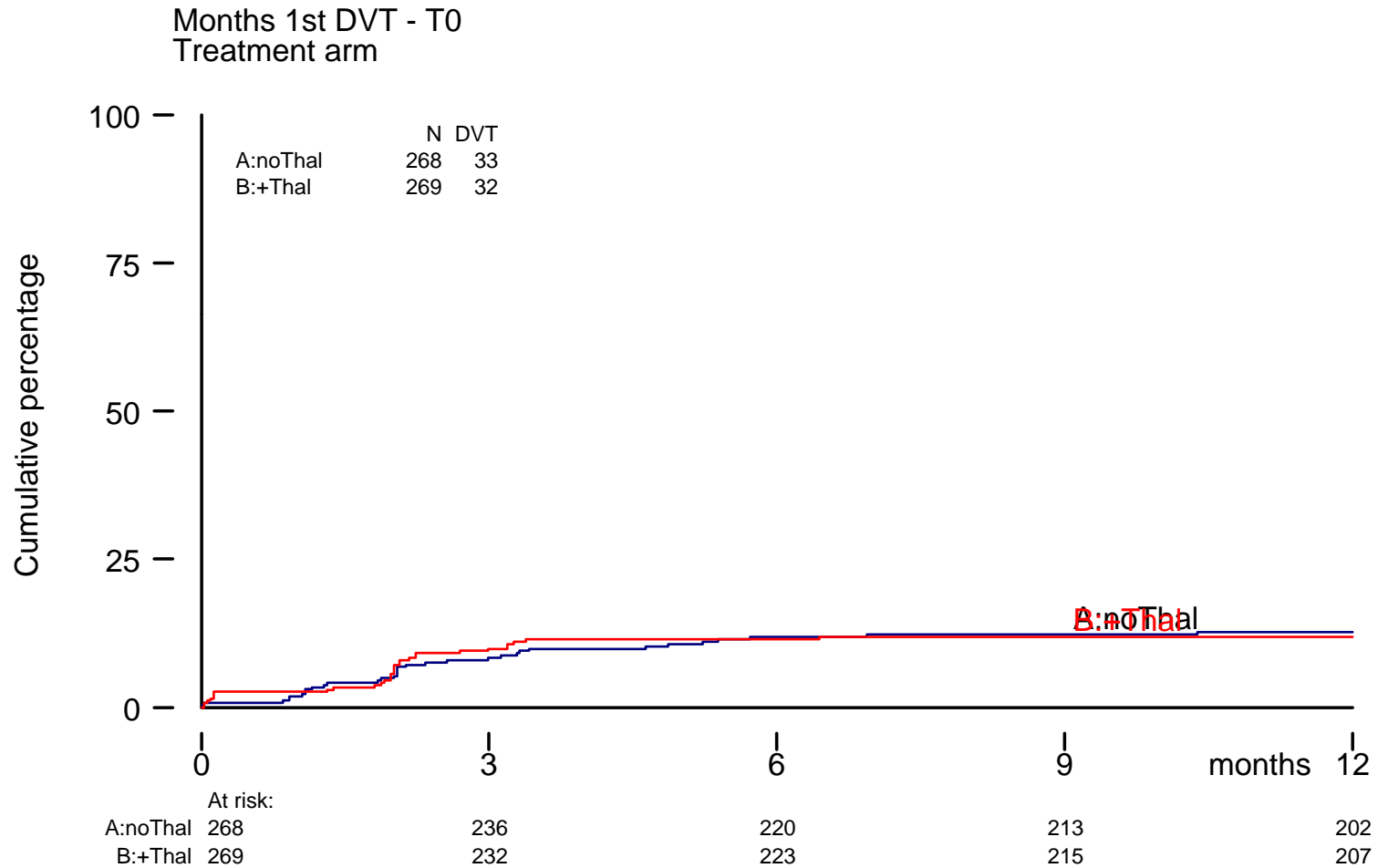
- 44%
- 30%
- 21%

Toxicity

	<u>Arm A (%)</u>	<u>Arm B (% , thal)</u>	<u>P</u>
CTC any 3/4	23	28	ns
Neurology 2 3/4	8 8	10 4	ns ns
Infections 2 3/4	7 10	7 11	ns ns
DVT < 3 months <12 months	8 13	10 12	ns ns

patients received LMWH during thalidomide induction

DVT during first 12 months



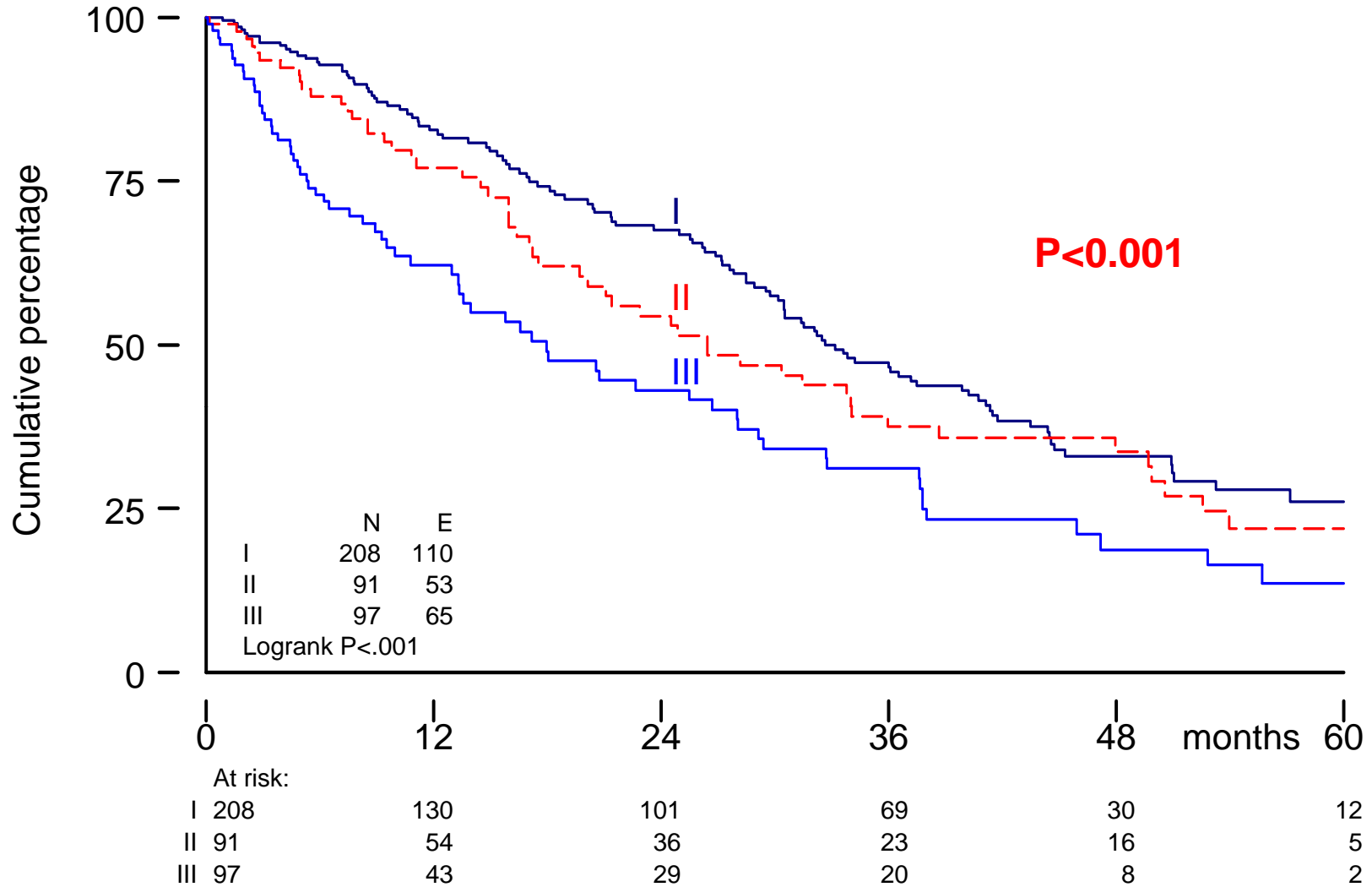
Adverse prognostic factors

Multivariate analysis

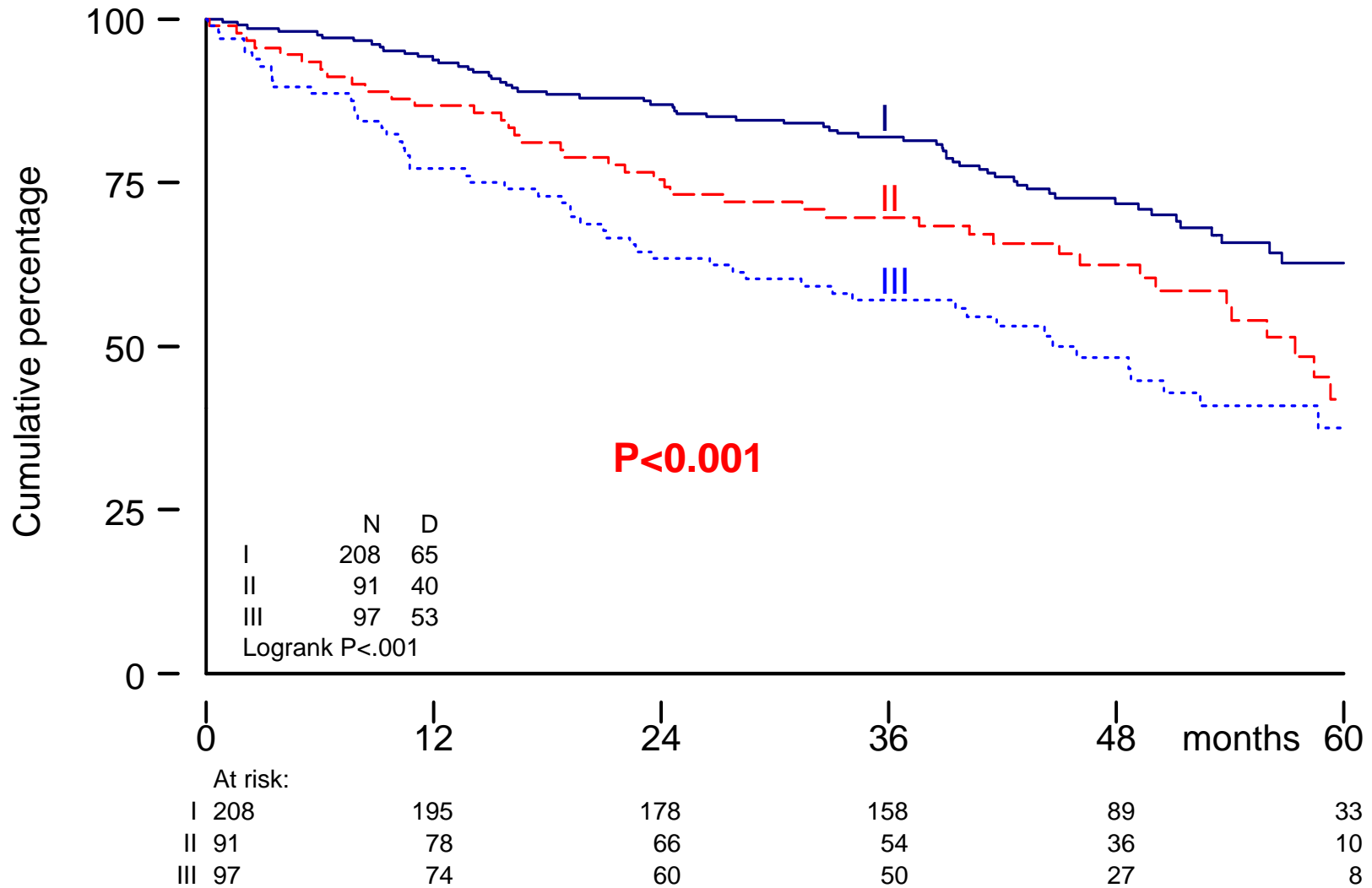
	CR	EFS	PFS	OS
age	ns	ns	ns	ns
stage	ns	ns	ns	ns
LDH	0.9	0.00008	0.0001	0.00001
IgA	0.4	0.5	0.01	0.001
λ	0.8	0.4	0.4	0.08
ISS II	0.6	0.4	0.8	0.1
ISS III	0.02	0.006	0.8	0.0005
Del 13	0.4	0.8	0.4	0.8

Thalidomide did not overcome unfavourable factors

EFS depending on ISS



OS depending on ISS



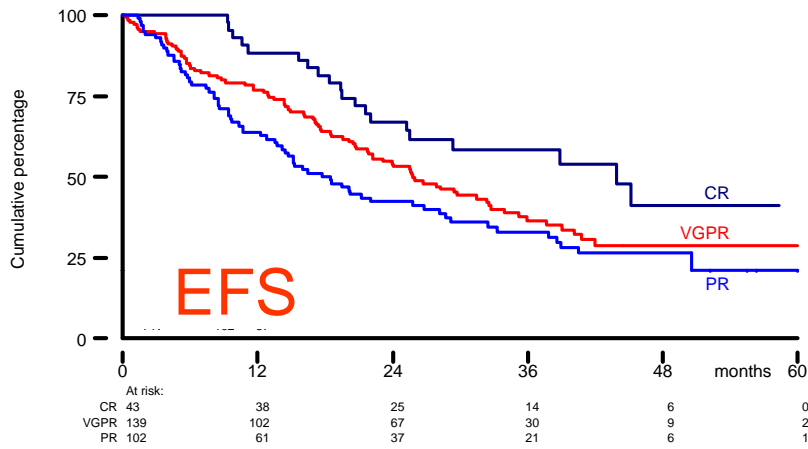
1 Dec 2008 - 09:32:45

Landmark analysis

best response achieved within 12 months

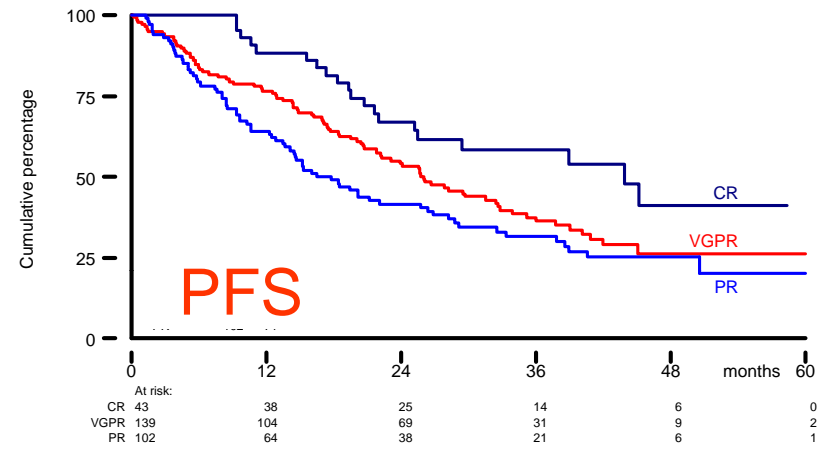
on

EFSC: EFS, [mo] (censored at alloSCT) [start = 12 mo]
Best response within 12 months



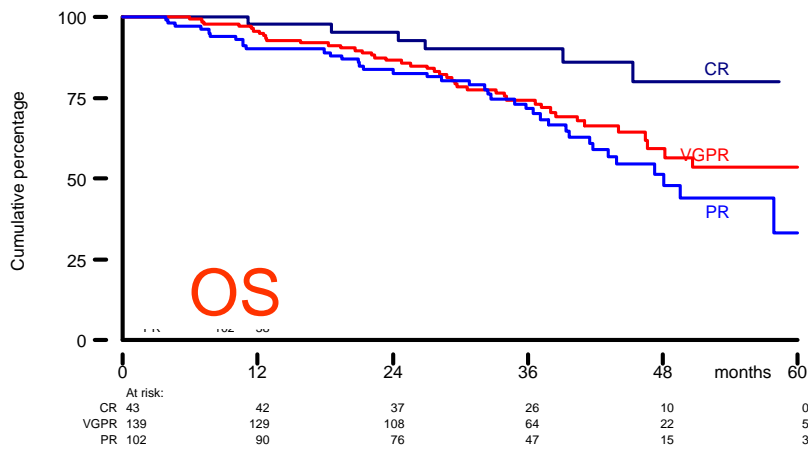
25 Nov 2008 - 11:05:42

PFS: Progression free survival [m] [start = 12 mo]
Best response within 12 months



25 Nov 2008 - 11:05:43

OS: Overall survival [m] [start = 12 mo]
Best response within 12 months

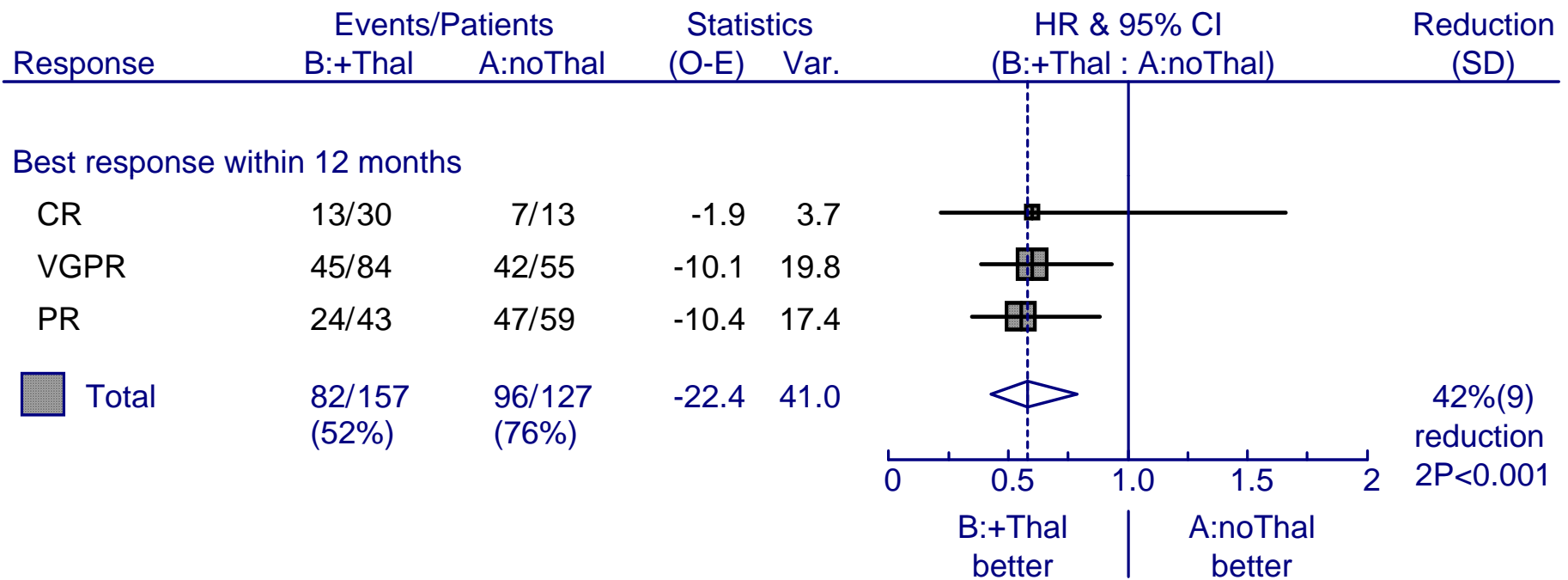


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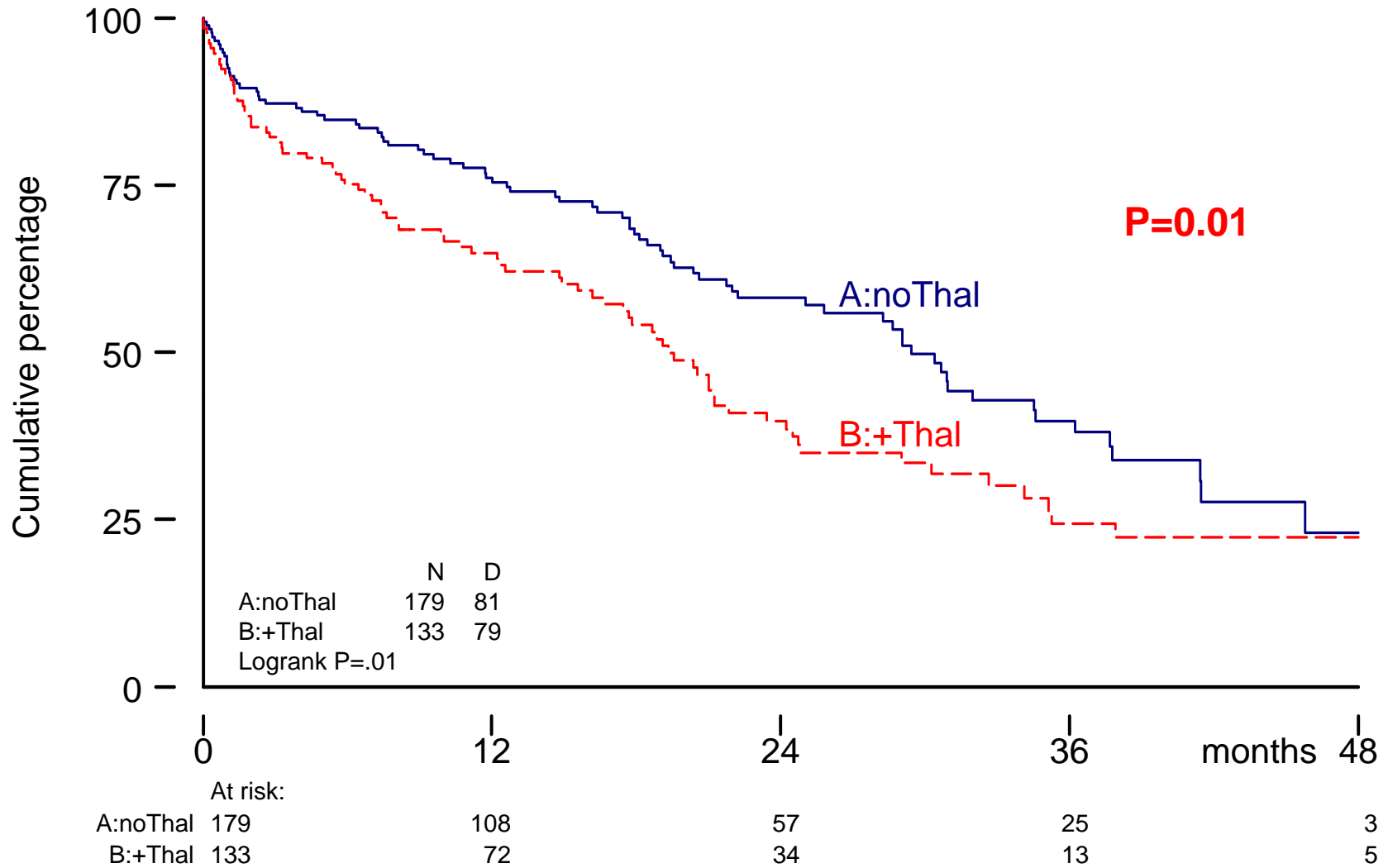
PFS by response

PFS from 12 months by response



Also patients achieving a VGPR/CR benefit from thalidomide maintenance with regard to PFS

Reduced OS from relapse after Thal exposure



The most effective strategy of maintenance with thalidomide is still debated

- Both MP-T studies of IFM with **limited thalidomide** exposure prolong OS .
- Nordic, Gimema, Hovon MP-T studies with **thalidomide until relapse** do not improve OS
- In Tunesian study **limited thalidomide** maintenance (6 months after HDM) improves OS
- In Total therapy 2 and Hovon 50, **thalidomide until relapse** does not improve OS

*consolidation better than maintenance?
Impact of response after intensification?*

Conclusions

- Thalidomide combined with intensive therapy improves EFS, PFS but not OS
- Achievement of a CR is the most determinant factor for prolonged PFS and OS.
→ *improvement of CR is the ultimate goal*
- The role of maintenance versus consolidation therapy (*versus quality of response*) of thalidomide (novel agents) is still debated



Participating hospitals (48)

B-Leuven-Gasthuisberg
NL-Amersfoort-Eemland
NL-Amsterdam-AMC
NL-Amsterdam-AVL
NL-Amsterdam-OLVG
NL-Amsterdam-Slotervaart
NL-Amsterdam-VUMC
NL-Apeldoorn-Gelre, Lukas
NL-Arnhem-Rijnstate
NL-Breda-Amphia, Langendijk
NL-Breda-Amphia, Molengracht
NL-Brunssum-Atrium
NL-Delft-RdeGraaf
NL-Delfzijl-Delfzicht
NL-Den Bosch-Bosch MC
NL-Den Bosch-Carolus
NL-Den Haag-Leyenburg
NL-Deventer-Ziekenhuizen
NL-Dordrec-Schweitzer-Dortwijk
NL-Dordrech-Schweitzer-Amstelw
NL-Eindhoven-Catharina
NL-Enschede-MS Twente
NL-Gouda-Groene Hart
NL-Groningen-AZG
NL-Haarlem-Kennemer
NL-Heerlen-Atrium
NL-Hengelo-SZ Twente
NL-Leeuwarden-MC
NL-Leiden-LUMC
NL-Leidschendam-
NL-Maastricht-AZM
NL-Nieuwegein-Antonius Ng
NL-Nijmegen-Canisius
NL-Nijmegen-Radboud
NL-Roosendaal-Franciscus
NL-Rotterdam-Clara
NL-Rotterdam-EMC
NL-Rotterdam-EMC Daniel
NL-Rotterdam-Franciscus
NL-Rotterdam-Zuider
NL-Sittard-Maasland
NL-Utrecht-Diakonessen
NL-Utrecht-UMCU
NL-Veldhoven-Maxima
NL-Venlo-Vie Curie
NL-Zaandam-De Heel
NL-Zwolle-Sophia
NL-Zwolle-Weezenlanden