Post-ASH Seminar

Genmab Powering Forward: Maximizing Pipeline Value

December 9, 2014
Live in San Francisco 12:00PM – 3:00PM PST
Via WebEx 9:30PM – 11:30PM CET

Genmab

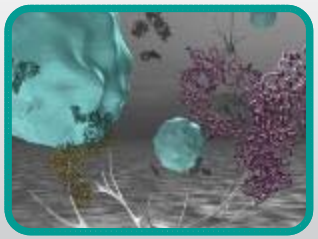
Forward Looking Statement

This presentation contains forward looking statements. The words “believe”, “expect”, “anticipate”, “intend” and “plan” and similar expressions identify forward looking statements. All statements other than statements of historical facts included in this presentation, including, without limitation, those regarding our financial position, business strategy, plans and objectives of management for future operations (including development plans and objectives relating to our products), are forward looking statements. Such forward looking statements involve known and unknown risks, uncertainties and other factors which may cause our actual results, performance or achievements to be materially different from any future results, performance or achievements expressed or implied by such forward looking statements. Such forward looking statements are based on numerous assumptions regarding our present and future business strategies and the environment in which we will operate in the future. The important factors that could cause our actual results, performance or achievements to differ materially from those in the forward looking statements include, among others, risks associated with product discovery and development, uncertainties related to the outcome of clinical trials, slower than expected rates of patient recruitment, unforeseen safety issues resulting from the administration of our products in patients, uncertainties related to product manufacturing, the lack of market acceptance of our products, our inability to manage growth, the competitive environment in relation to our business area and markets, our inability to attract and retain suitably qualified personnel, the unenforceability or lack of protection of our patents and proprietary rights, our relationships with affiliated entities, changes and developments in technology which may render our products obsolete, and other factors. Further, certain forward looking statements are based upon assumptions of future events which may not prove to be accurate. The forward looking statements in this document speak only as at the date of this presentation.

Agenda

12:30PM	**Welcome**	Jan van de Winkel, PhD, *President & CEO*
12:40PM	**News from the Clinic**	
12:40PM	Daratumumab	Dr. Paul Richardson, *Dana Farber Cancer Institute, Boston* Prof. Torben Plesner, *Vejle Hospital, Arhus* Prof. Antonio Palumbo, *University of Torino*
	Daratumumab Q&A	
1:30PM	Ofatumumab	Prof. Marinus van Oers, *Academic Medical Center, Amsterdam*
	Ofatumumab Q&A	
1:45PM	HuMax-TF-ADC	Steen Lisby, MD, *Sr Medical Director*
1:50PM	**Pre-clinical Pipeline: The Antibody Experts**	
1:50PM	Building an Innovative Pipeline	Jan van de Winkel
1:55PM	Antibody Engineering & Next Generation Therapeutics	Prof. Thomas Valerius, *University Hospital Schleswig-Holstein, Kiel*
2:05PM	The Year Ahead	Jan van de Winkel
2:10PM	**Q&A**	
2:30PM	**Refreshments**	

Antibody Innovation Generating World Class Products



Focus on Cancer

- Differentiated human antibodies
- Track record breakthrough therapeutics

Robust Product Pipeline

- Ofatumumab – cancer & autoimmune potential (marketed as Arzerra® in various CLL indications)
- Daratumumab blockbuster potential
- HuMax®-TF-ADC in Phase I solid cancers

Passion for Innovation

- World class antibody know-how
- Proprietary technologies – DuoBody® & HexaBody™
- Innovative pre-clinical pipeline

Partnerships → Product Ownership

- Key collaborations drive current pipeline
- Product opt-ins + retain products for future value
- Well capitalized

2014 Progress Across All Business Areas

Daratumumab

Ofatumumab

Pipeline

Partnerships

Technology

Finances

Rapidly Advancing Daratumumab

Daratumumab

- 5 new Phase III studies announced
- Data from 3 studies
- Pre-clinical data in non-MM indications
- Announced Phase II study in NHL
- $57 M in milestones from Janssen

Maximizing the Value of Ofatumumab

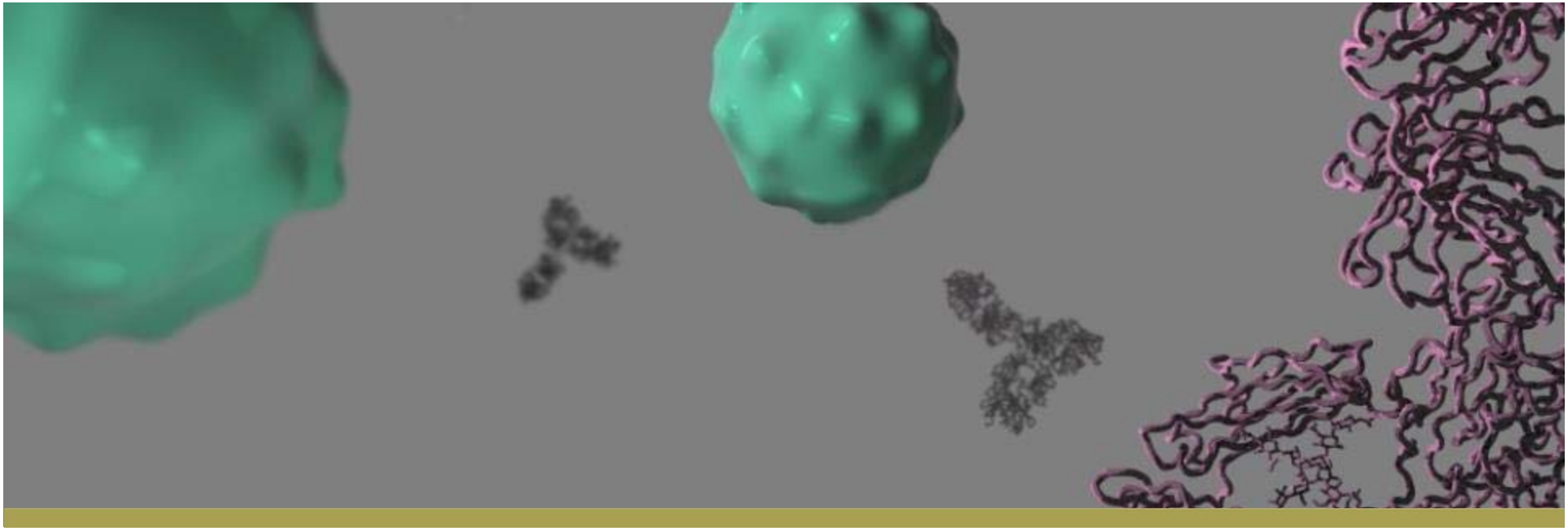
Ofatumumab

- 1st line CLL label expansion & launch
- Positive Phase III maintenance data in relapsed CLL
- Data from 2 other Phase III studies
- GSK to move RRMS into Phase III
- Transfer agreement with GSK & Novartis

Progressing Our Pipeline and Technologies

Pipeline & Technology

- HuMax-TF-ADC in Phase I
- New collaboration with Seattle Genetics for HuMax-AXL-ADC
- New DuoBody platform collaborations
- DuoBody collaborations generated cash of $13 M
- 2 HexaBody platform collaborations



News from the Clinic

Daratumumab

Presented by Dr. Paul Richardson, *Dana Farber Cancer Institute*

Genmab

DANA-FARBER
CANCER INSTITUTE

New Directions in Treating Multiple Myeloma in the Era of Novel Agents

Paul G. Richardson, MD

RJ Corman Professor of Medicine,
Harvard Medical School
Jerome Lipper Multiple Myeloma Center
Dana-Farber Cancer Institute
Boston, MA

Multiple Myeloma Epidemiology

- Multiple myeloma represents 10-15% of all hematologic malignancies[1]
- Incidence in US:
  Estimated 24,050 new cases in 2014[2]
  - Median age at diagnosis is 69 years
- Prevalence in US:
  - 83,367 people living with myeloma [a]
- ~ 11,000 deaths per annum

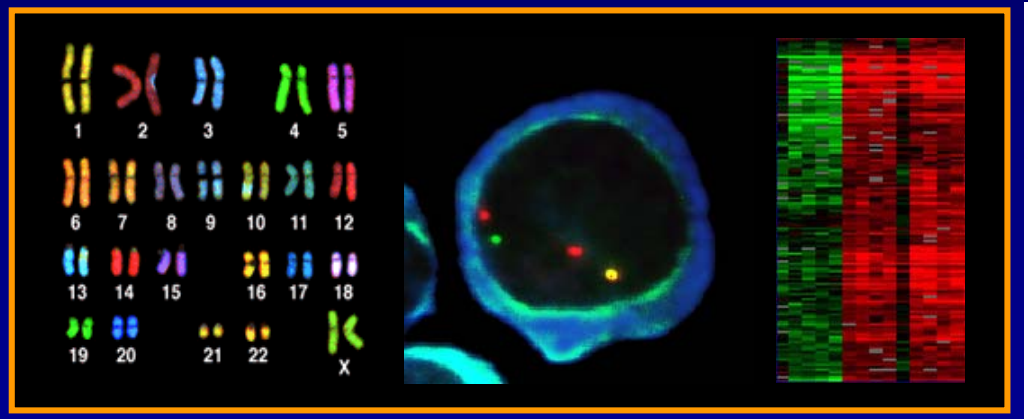
[a] Prevalence data are for 2011.

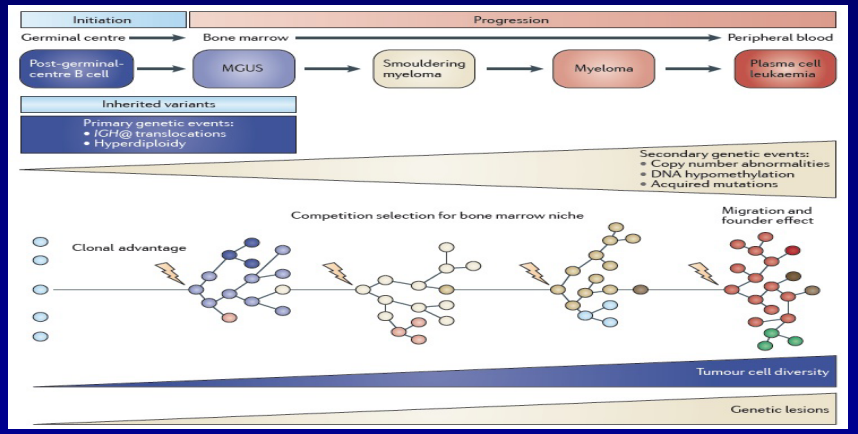
1. Raab MS, et al. *Lancet*. 2009;374:324-39; 2. SEER Cancer Statistics Factsheets: Myeloma. National Cancer Institute. Bethesda, MD, http://seer.cancer.gov/statfacts/html/mulmy.html.

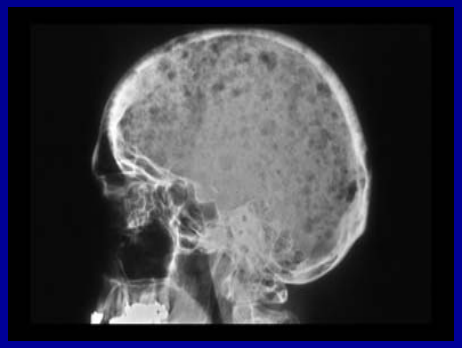
MULTIPLE MYELOMA
…not just one disease!

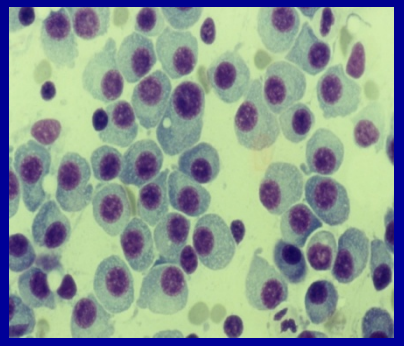
- Risk stratification, recognition of clonal heterogeneity
- Individualization of treatment, advent of novel therapies

3 decades









Drach J, ASH 2012

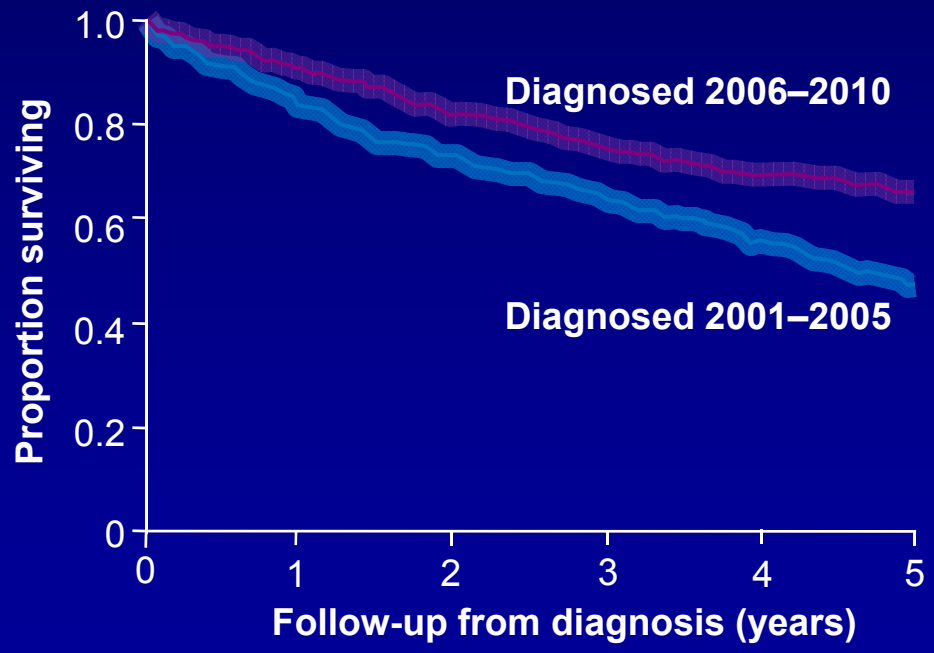
Morgan et al. *Nat Rev Cancer* 2012;12:335-348

Progress and Challenges in the Treatment of MM

- **Progress**
  - Better understanding of disease biology
  - Substantial improvements in outcome due to availability of new effective therapies
  - Therapeutic Backbone of Novel Agents, and specifically PI's and IMiDs, in addition to SCT and continued role of conventional cytotoxics ~
    - Potential for MM to become a chronic disease in some pts
  - Learnings in the management of adverse events, comorbidities, handling of novel agents
- **Challenges**
  - MM remains incurable in majority of pts
  - Increasing symptom burden due to disease and cumulative effects of treatments
  - Managing balance of disease control and quality of life
  - Novel mechanisms of action for next generation agents urgently needed

Continued Improvement in Survival Since the Introduction of Novel Agents

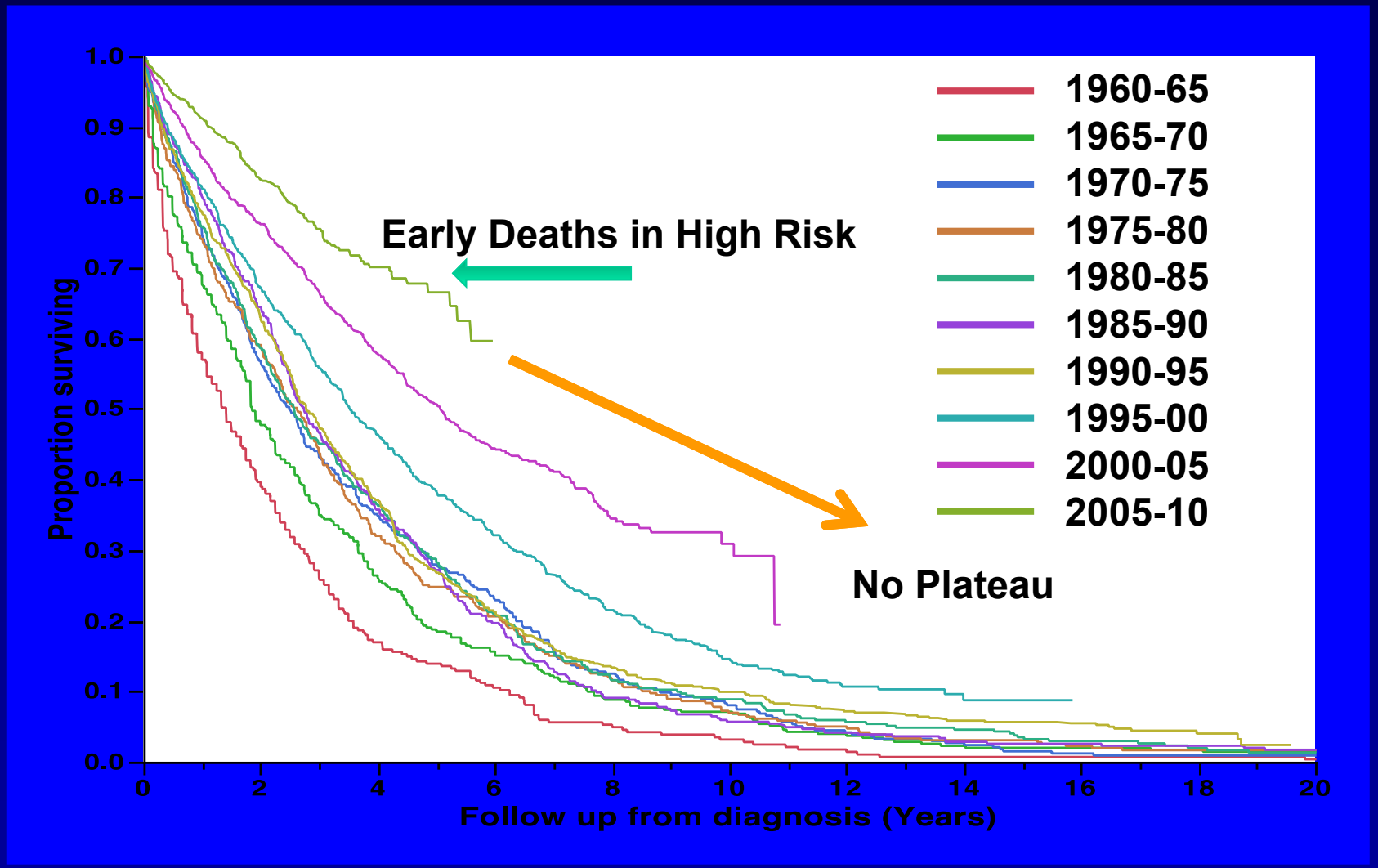
- 1,056 pts grouped into 2001–2005 and 2006–2010 cohorts
- Survival improved over time, particularly in pts aged > 65 years (p = 0.001)



Survival	2001–2005	2006–2010	p
Median OS, years	4.6	NR	0.001
1-year survival, %	83	90	
5-year estimated OS, %			
Overall	48	66	
> 65 years	31	56	0.001
< 65 years	63	73	NS

Kumar SK, et al. *Leukemia* 2014.

Multiple Myeloma Survival Improving With New Drugs: But All Pts Still Relapse After IMiD and PI Failure



Adapted from Kumar et al *Leukemia* 2014

Recommended Induction Regimens: USA/EU Perspective

Induction with

3-drug regimens
Bortezomib/dex +
IMiD/alklyator/anthracycline
VTD* / RVD
VCD
PAD*
CTD*

2-drug regimens
Bortezomib/dex*
RD/Rd

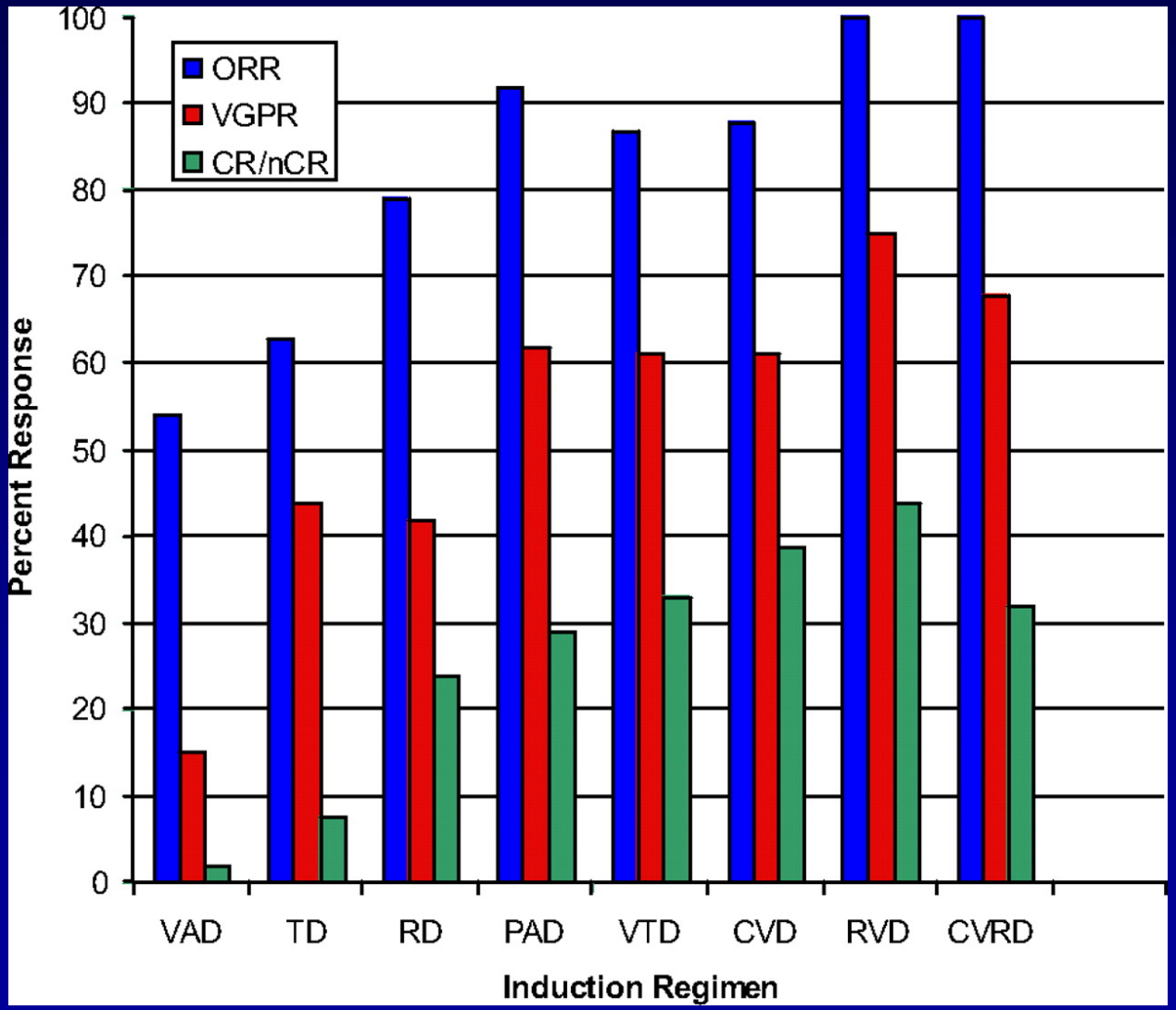
Stem cell harvest (G-CSF, Chemo?)
High-dose melphalan (1? 2?)
→ Stem cell infusion

Strong preference for 3-drug regimens

*Data available from Phase III randomized clinical trials

Ludwig et al. *The Oncologist* 2012; 17(5):592-606

Combinations in the Upfront Treatment of MM

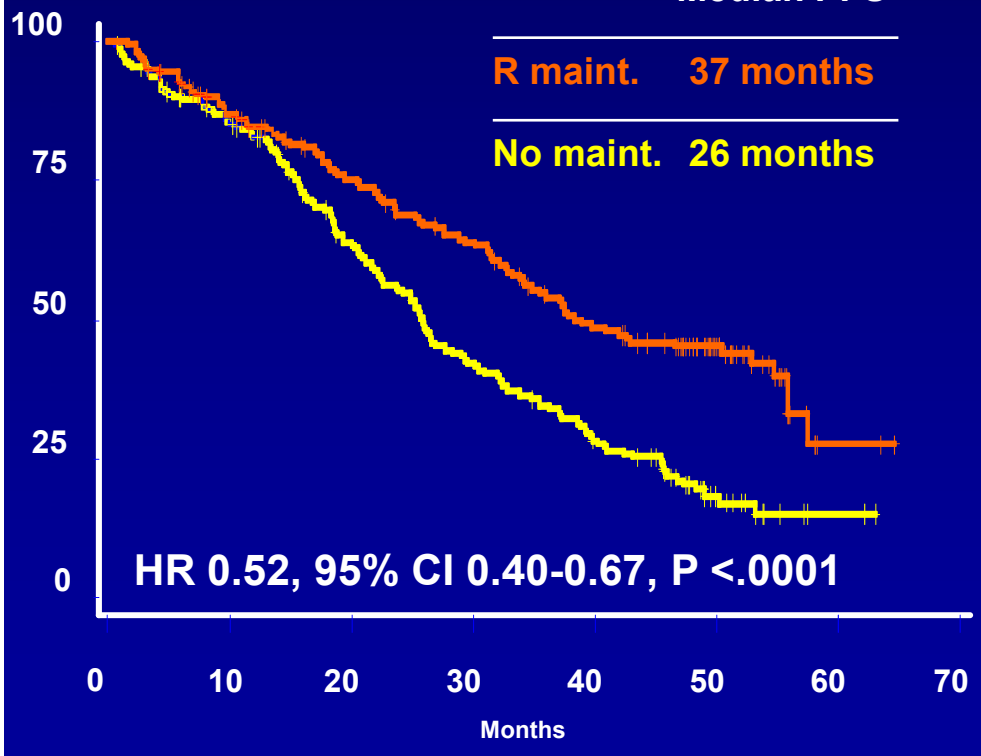


Stewart AK, Richardson PG, San Miguel JF *Blood* 2009

Revlimid maintenance vs No maintenance
Palumbo et al, ASCO 2013; *NEJM* 2014

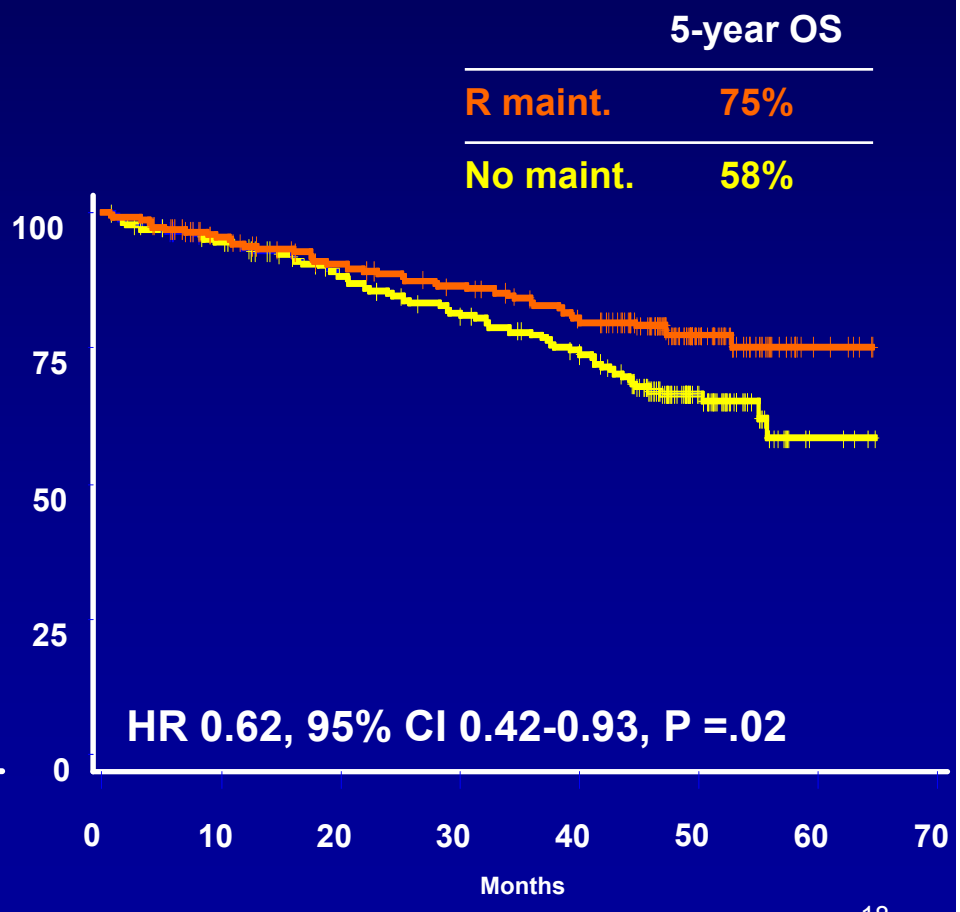
Progression-free survival

48% reduced risk of progression



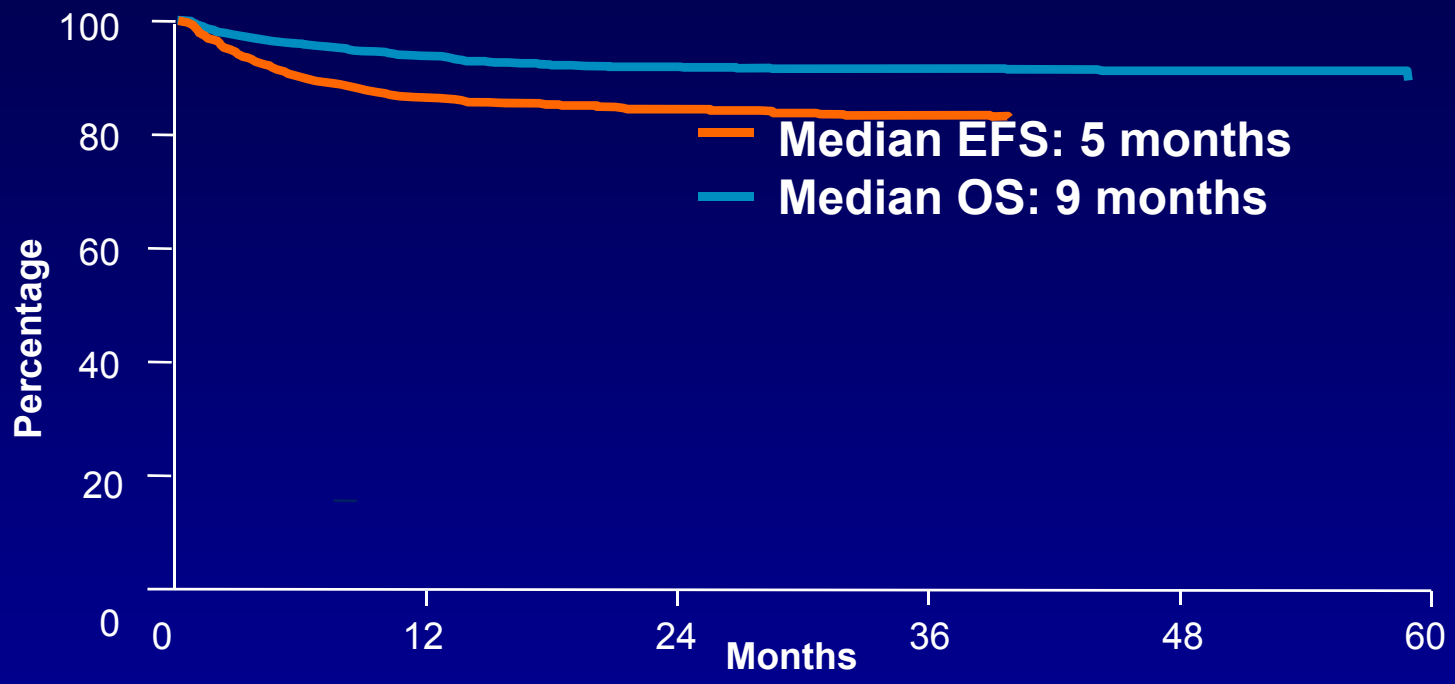
Overall survival

38% reduced risk of death



R, lenalidomide

Poor Survival Outcomes for Patients With Advanced RRMM



- For patients (N = 286) refractory to Bort and relapsed/refractory or ineligible for immunomodulatory drugs[a]
  - 49% had no response to the first treatment
  - Median OS was 12 months for patients receiving at least one treatment, and 3 months for patients receiving no treatment

[a] Lenalidomide and/or thalidomide.
Bort, bortezomib; EFS, event-free survival; OS, overall survival.

Kumar SK, et al. *Leukemia.* 2012;26:149–157.

Bortezomib and Lenalidomide Therapy

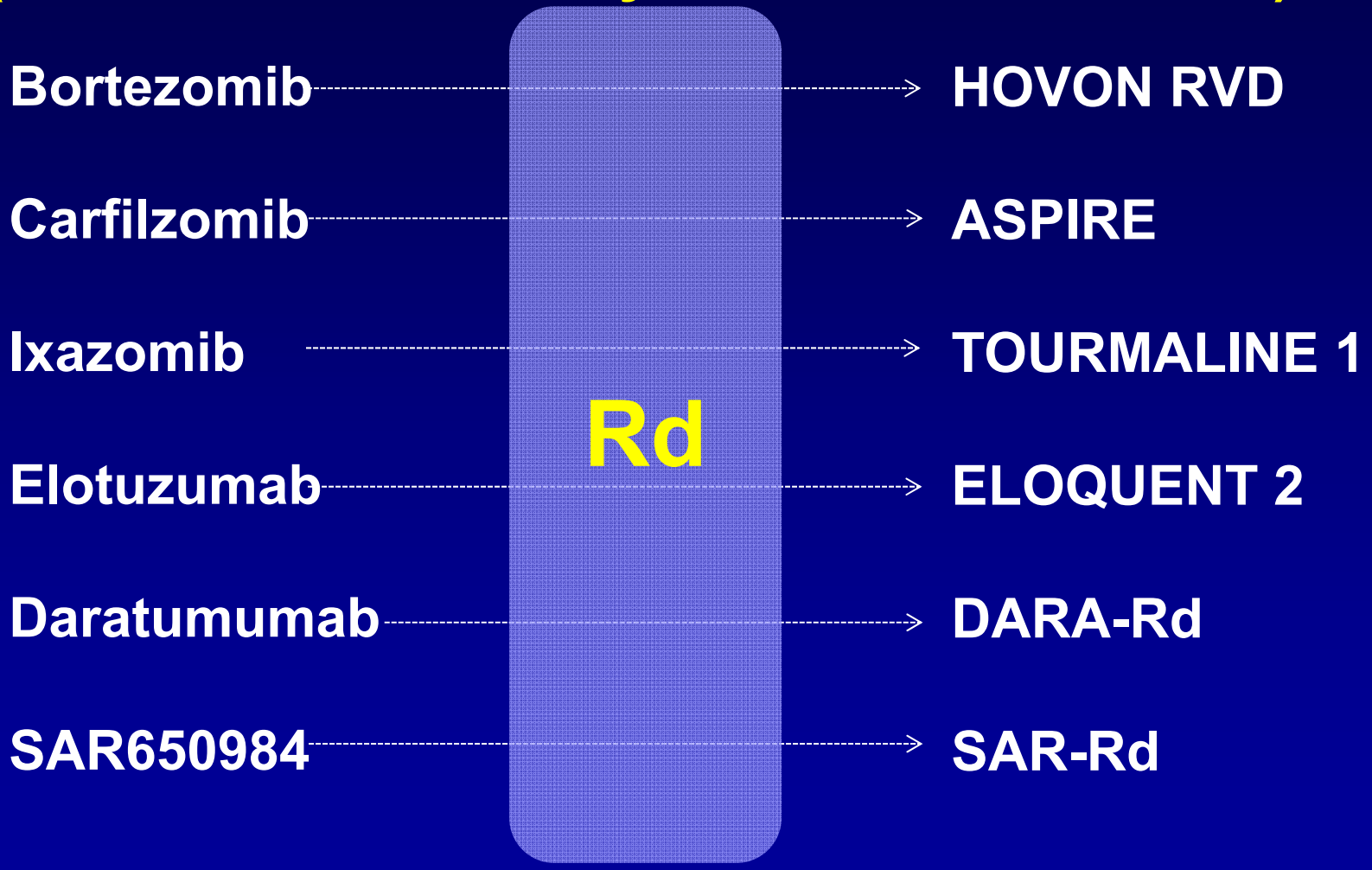
- Lenalidomide induces caspase 8 mediated apoptosis of MM cells in BM *in vitro* and *in vivo*; Dex (caspase 9) enhances response.
- Synergistic MM cell toxicity of lenalidomide (caspase 8) with Bortezomib (caspase 9 > 8) *in vitro* and *in vivo* (dual apoptotic signaling).
- Phase I trial (RVd) in RRMM shows that majority of pts refractory to either agent alone respond to the combination (ORR 58%, OS > 3 years), and manageable toxicity.
- Phase I-II trial in NDMM (n=66) show 100% response with 74% VGPR or better, 52% CR/nCR when used as initial therapy.
- Phase II study in RRMM (n=60) confirms high ORR (65%) and favorable OS (~ 3 years), with favorable tolerability.

Richardson PG, et al. *J Clin Oncol* 2009;27:5713-9.
Richardson PG, et al. *Blood* 2010;116:679-86.
Richardson PG, *et al. Blood* 2014;123:1461-9.

Selected Novel Agents Currently Available and/or Under Investigation for RR MM

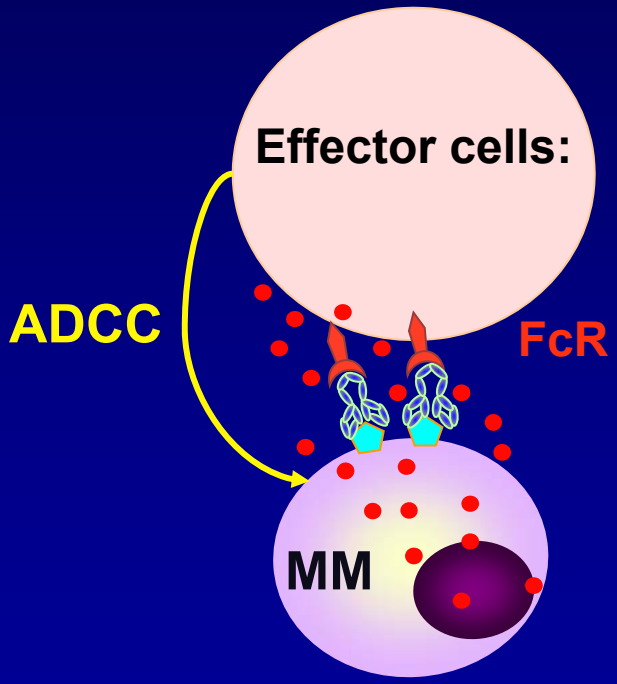
Class	First generation	Next generation
Immunomodulatory drugs	Lenalidomide (p.o.)	Pomalidomide (p.o.)
Proteasome inhibitors	Bortezomib (i.v./s.c.) [n.b. recent FDA approval for re-treatment]	Carfilzomib (i.v.) Ixazomib [MLN9708] (p.o.) Oprozomib [ONYX0912] (p.o.) Marizomib [NPI-0052] (i.v.)
Others small molecule innhibitors including: HDACi, AKTi, BTKi	Vorinostat, Panobinostat, Romidepsin, Ricolinostat Ibrutinib	Rational combinations with 'first generation' novel agents and next generation agents ['novel + novel'] e.g. Bromodomain Inhibitors/IMiDs
Monoclonal Antibodies	Elotuzumab, Daratumumab SAR650984	Immune Therapies/IMiDs/MoAbs (incl. checkpoint inhibitors e.g. PD1, PDL1 MoAbs)
Alkylating Agents, Other Cytotoxics (e.g. KSPi)	Bendamustine, others; Array 520 TH 302, Melflufen	Combining with PIs and IMiDs

LEN and Bortezomib- based Triple Therapy Combinations in RRMM (and now under study in Phase 1/2/3 trials)



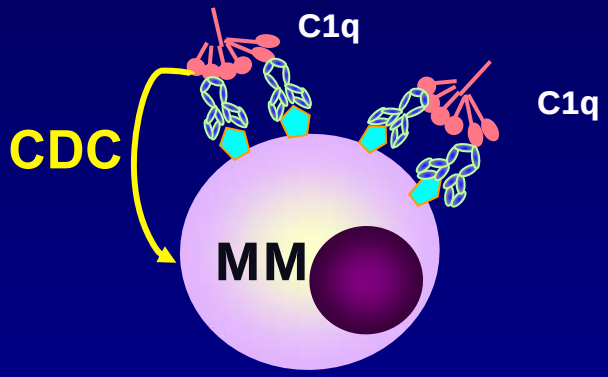
MAb-Based Therapeutic Targeting of Myeloma

Antibody-dependent Cellular cytotoxicity (ADCC)



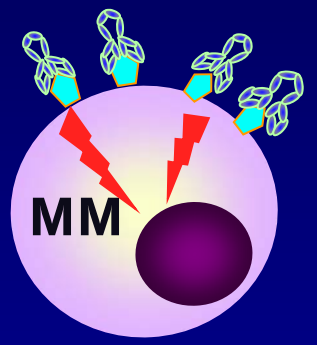
- Lucatumumab or Dacetuzumab (CD40)
- Elotuzumab (CS1; SLAMF7)
- Daratumumab, SAR650984 (CD38)
- XmAb®5592 (HM1.24)

Complement-dependent Cytotoxicity (CDC)



- Daratumumab
- SAR650984 (CD38)

Apoptosis/growth arrest via targeting signaling pathways



- huN901-DM1 (CD56)
- nBT062-maytansinoid (CD138)
- Siltuximab (1339) (IL-6)
- BHQ880 (DKK1)
- RAP-011 (activin A)
- Daratumumab, SAR650984 (CD38)

Adapted from Tai & Anderson Bone Marrow Research 2011

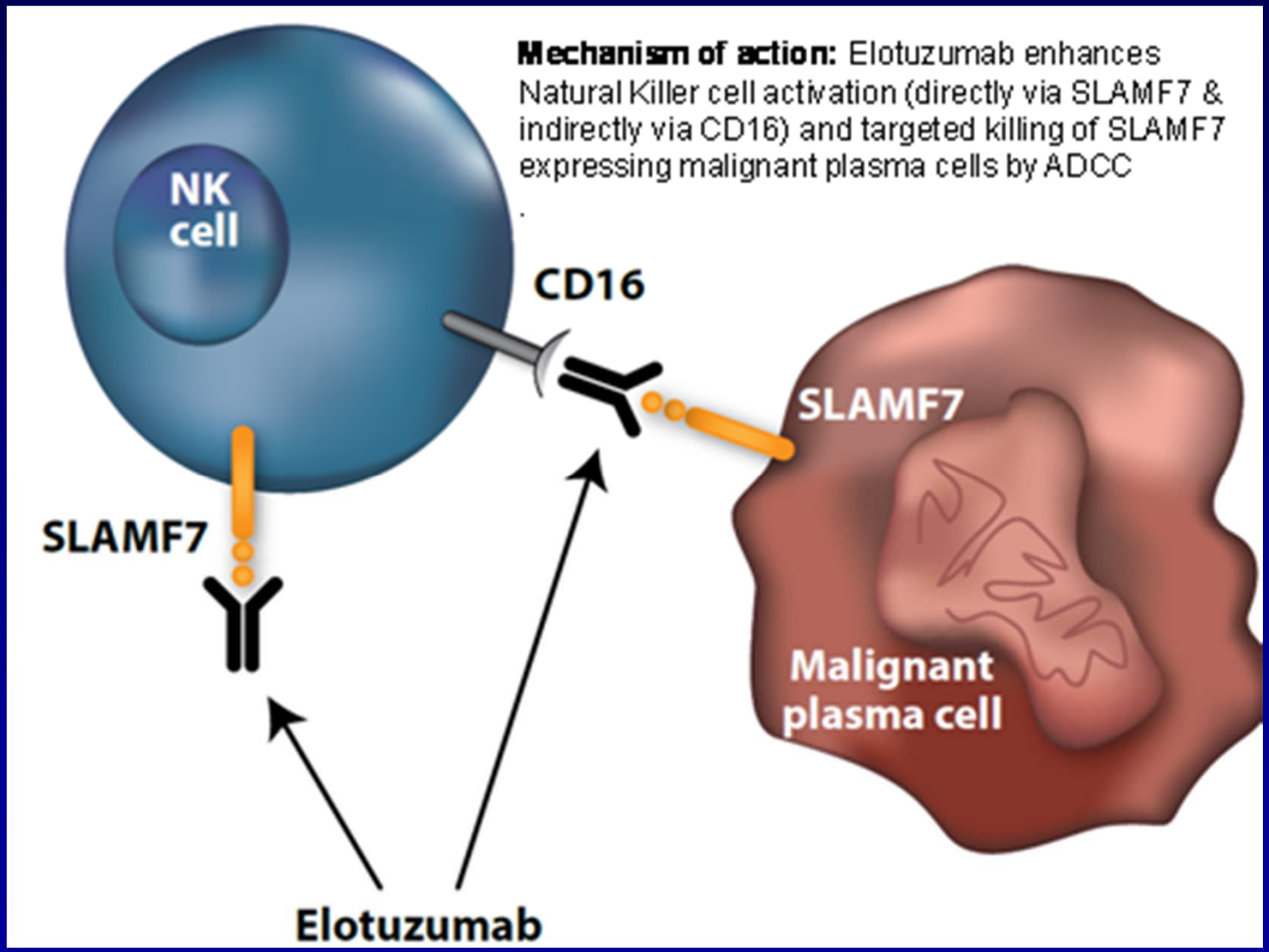
Monoclonal Antibodies in MM

Target	mAb	Stage of development
Surface molecules		
CS1/SLAMF7	Elotuzumab	Phase 2/3
CD38	Daratumumab	Phase 1/2/3
	SAR650984	Phase 1/2
	MOR202	Phase 1/2
CD74	Milatuzumab	Phase 1/2
CD40	Dacetuzumab	Phase 1
CD56	Lorvotuzumab mertansine	Phase 1
CD138	BT062	Phase 1
Signaling molecules		
IL-6	Siltuximab	Phase 3
RANKL	Denosumab	Phase 3
B cell activating factor (BAFF)	Tabalumab	Phase 2/3
VEGF	Bevacizumab	Phase 2
DKK1	BHQ880	Phase 2

Richardson et al. et al. IMW 2013 (Abstract P-214), poster presentation
Plesner et al. ASH 2013 (Abstract 1987), poster presentation
Martin et al. ASH 2013 (Abstract 284), oral presentation
http://www.clinicaltrials.gov/ct2/show/NCT00421525
http://www.clinicaltrials.gov/ct2/show/NCT00079716

http://www.clinicaltrials.gov/ct2/show/NCT00346255
http://www.clinicaltrials.gov/ct2/show/NCT01001442
Wong et al. ASH 2013 (Abstract 505), oral presentation
Hageman et al. Ann Pharmacother 2013;47:1069-74

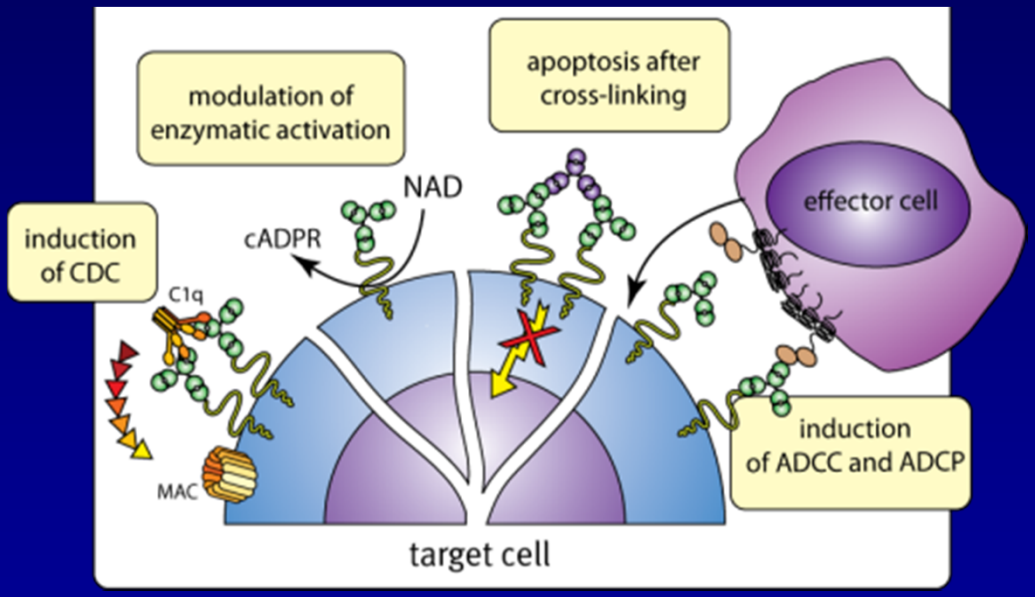
Elotuzumab in MM - MoA



Daratumumab in MM - MoA

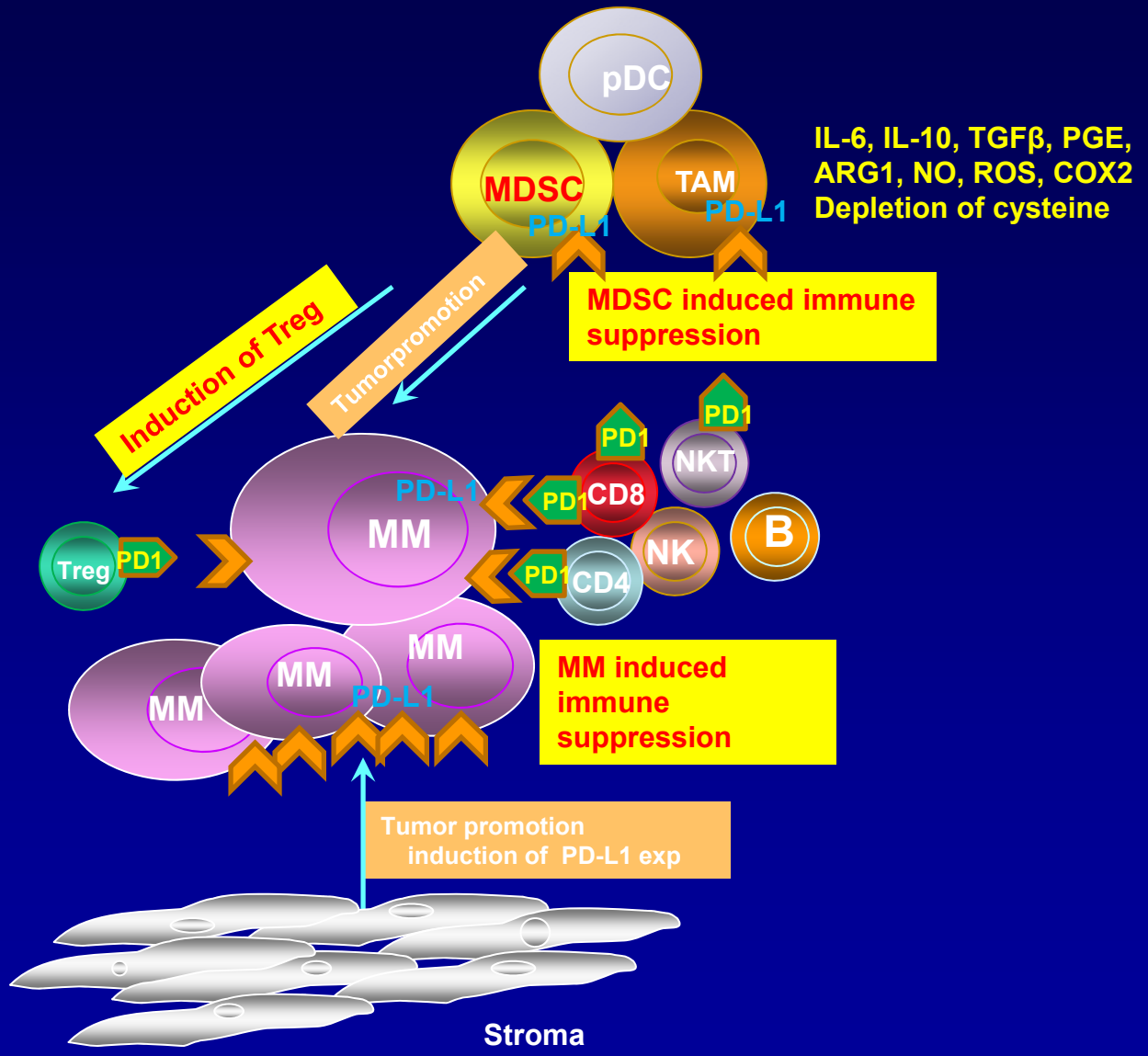
Daratumumab

- A human mAb that targets CD38-expressing tumor cells



- Antibody-dependent cell-mediated cytotoxicity (ADCC)
- Antibody-dependent cellular phagocytosis (ADCP)
- Complement-dependent cytotoxicity (CDC)
- Apoptosis

Immune Suppressive Microenvironment in MM

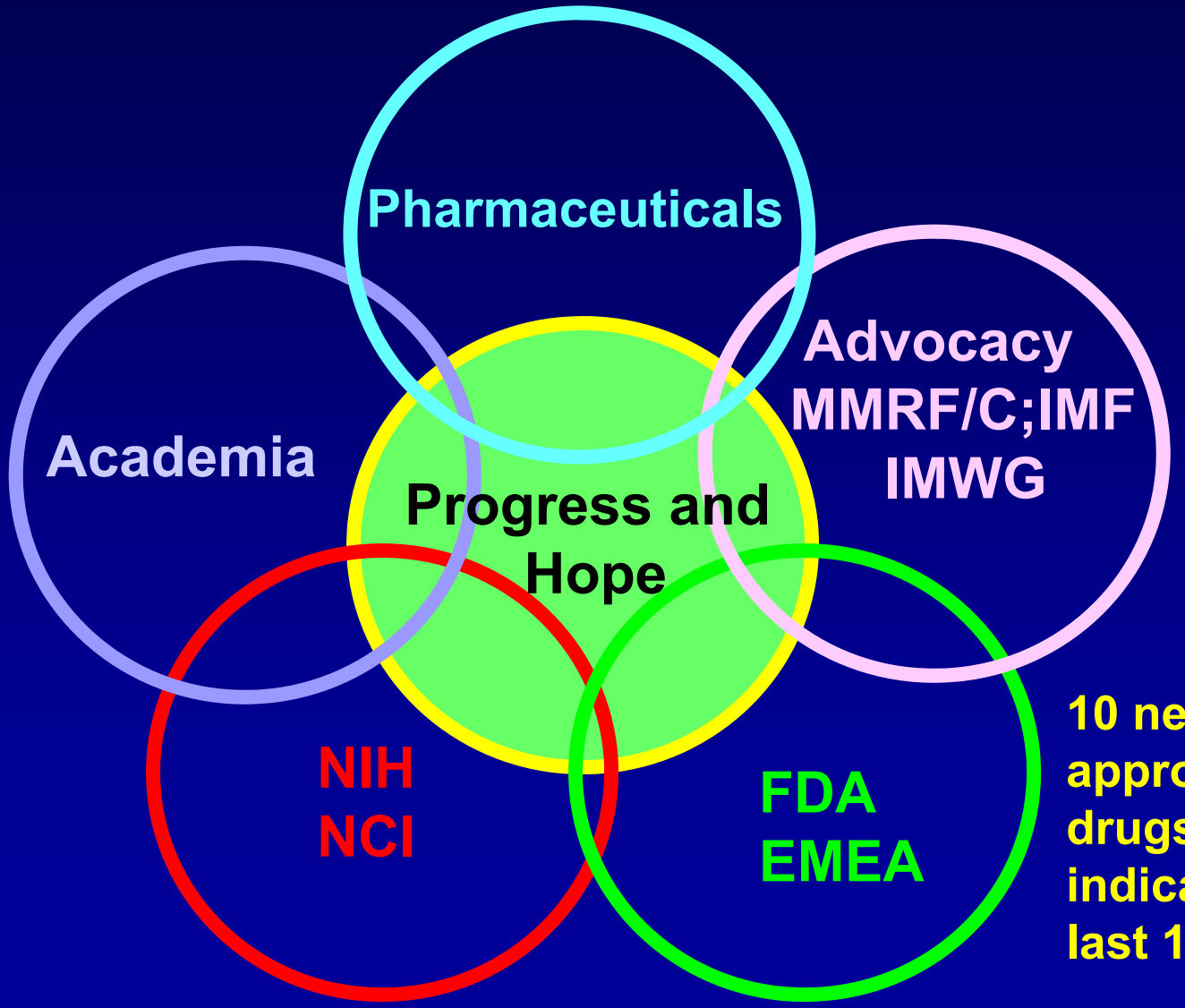


Görgün GT, et al. *Blood* 2013;121:2975-87.

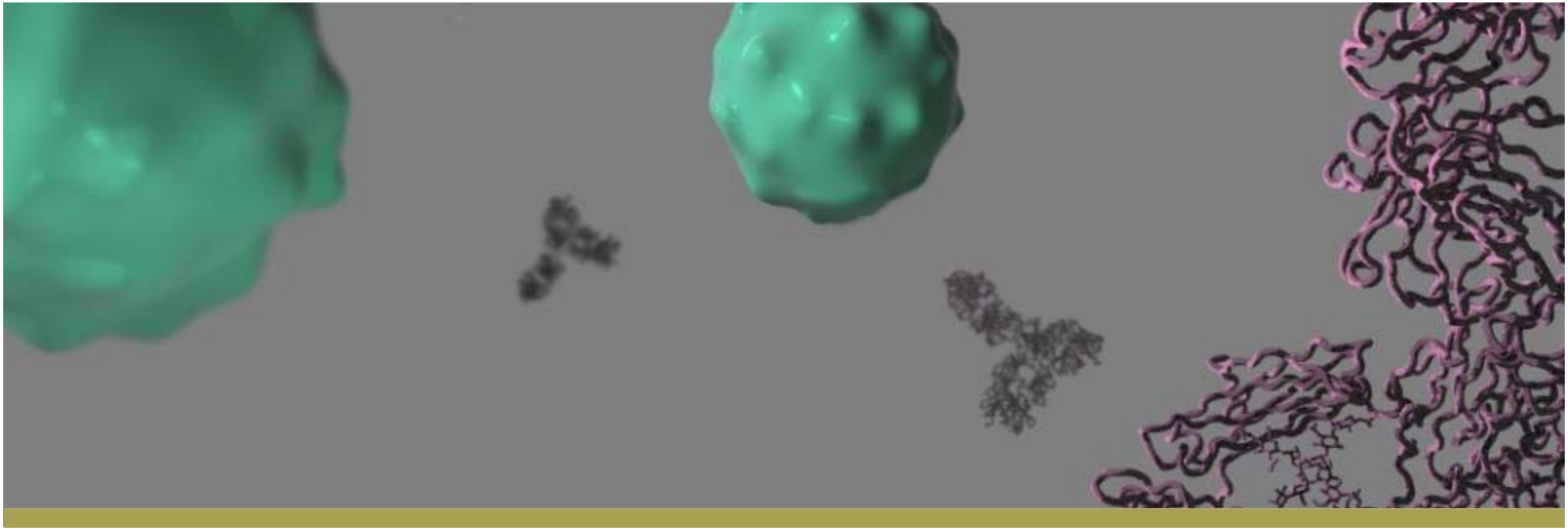
Next Generation Novel Agents In MM

- Innovations (PIs, IMiDs) to date have produced significant improvements in PFS and OS
- Next wave of therapies ~ mutation-driven, as well as plasma cell biology-related
- Baseline immune function appears to be a key barrier to success but may be targetable (e.g. use of PD1/PDL1 blockade)
- MoAbs have activity in high risk disease, and represent true new novel mechanisms, as do other immunotherapeutics (e.g. vaccines)
- Numerous other small molecule inhibitors show promise (e.g. HDAC, CXCR4, BCL, AKT, CDK, HSP 90, Nuclear Transport, KSP, BET bromodomain proteins/Myc, DUBs, MEK)
- New insights to mechanisms of drug action (e.g. IMiDs, PIs) are further expanding therapeutic opportunities with combinations

Ongoing MM Collaborative Model for Rapid Translation From Bench to Bedside



10 new FDA-approved drugs/combos/ indications in last 10 yrs



News from the Clinic

Daratumumab

Presented by Prof. Torben Plesner
Vejle Hospital

Genmab

Safety and Efficacy of Daratumumab with Lenalidomide and Dexamethasone in Relapsed, or Relapsed and Refractory Multiple Myeloma

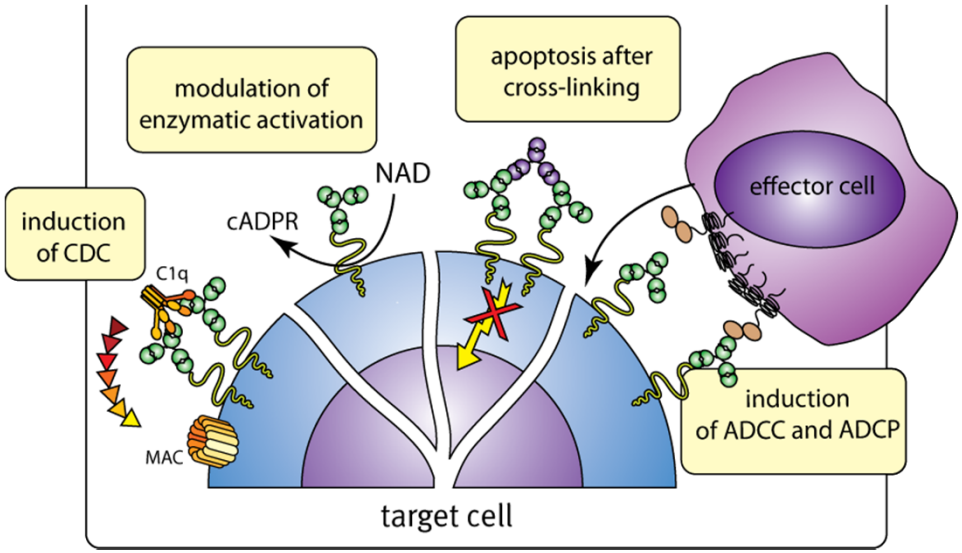
Torben Plesner[1], Hendrik-Tobias Arkenau[2], Henk M Lokhorst[3], Peter Gimsing[4], Jakub Krejcik[1], Charlotte Lemech[2], Monique Minnema[3], Ulrik Lassen[4], Jacob Laubach[5], Tahamtan Ahmadi[6], Howard Yeh[6], Mary Guckert[6], Jim Wang[6], Nikolai C. Brun[7], Steen Lisby[7], Linda Basse[7], Antonio Palumbo[8], Paul G. Richardson[5]

[1]Vejle Hospital, Vejle, Denmark; [2]Sarah Cannon Research Institute, London, United Kingdom; [3]UMC Utrecht, Utrecht, Netherlands; [4]Copenhagen University Hospital, Copenhagen, Denmark; [5]Dana-Farber Cancer Institute, Boston, MA; [6]Janssen Research & Development, LLC, Raritan, NJ; [7]Genmab A/S, Copenhagen, Denmark; [8]University of Torino, Torino, Italy

Background

Daratumumab

- A human mAb that targets CD38-expressing tumor cells
- DARA+LEN enhanced killing of MM cells *in vitro* and is hypothesized to lead to synergistically higher efficacy in clinical setting



- Antibody-dependent cell-mediated cytotoxicity (ADCC)
- Antibody-dependent cellular phagocytosis (ADCP)
- Complement-dependent cytotoxicity (CDC)
- Apoptosis

DARA: daratumumab; LEN: lenalidomide; mAB: monoclonal antibody; MM: multiple myeloma

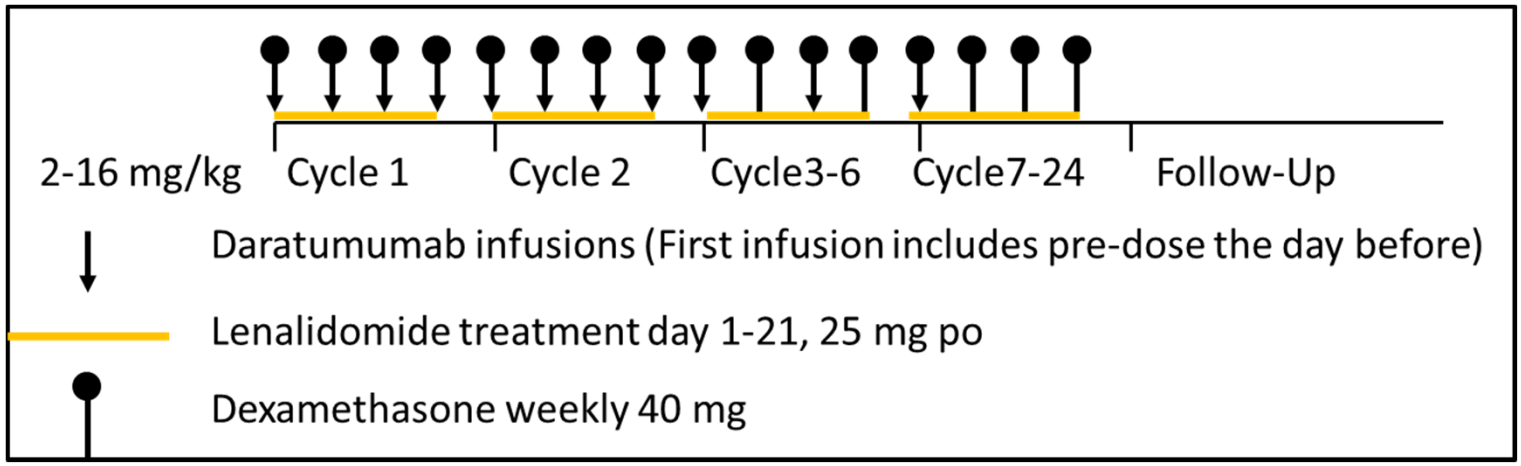
Background

- DARA plus LEN/DEX was well-tolerated in a very heavily pretreated patient population typical for MM (n=20) – *Data presented at* ASCO 2014
- Ongoing study with updated data for 45 patients (enrollment complete)

Objectives

- To establish the safety and efficacy profile of DARA in combination with LEN/DEX in relapsed, or relapsed and refractory (RR) MM

Study Design



Part 1: Dose escalation study (3X3 design) – 2-16 mg/kg dose; N=13

Part 2: Expansion cohort – 16 mg/kg dose; N=32

Key Eligibility

- Part 1: Relapsed and refractory MM following 2 – 4 prior lines of therapy
- Part 2: Relapsed and refractory MM following minimum 1 prior lines of therapy with no upper limit on number of prior therapy
- Measurable disease by M protein and light chain
- Adequate organ function
- Patients refractory or intolerant to LEN excluded

AE: adverse event; DARA: daratumumab; IMWG: International Myeloma Working Group; LEN: lenalidomide; MM: multiple myeloma; MR: minimal response; PD: progressive disease; PR: partial response

Results

Demographics & Baseline Characteristics

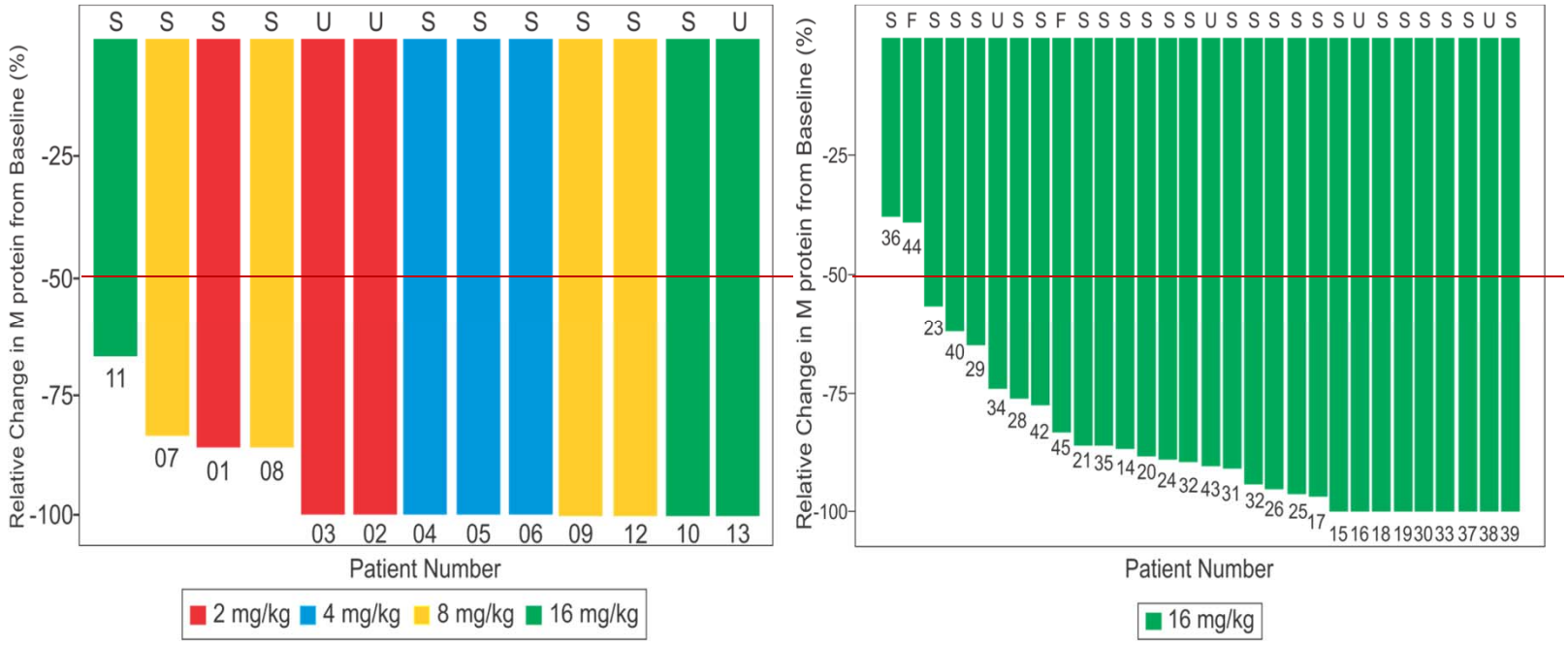
- Data from 45 patients (32 men,13 women) are evaluable for safety
  - 11 patients evaluated for accelerated infusion
- Data from 43 patients are evaluable for efficacy
- Median age: 61 (41 to 76) years
- Median prior lines of therapy: 2 (1 to 4)
  - 91% patients had prior exposure to PI (bortezomib)
  - 80% patients had prior exposure to IMiD (lenalidomide and thalidomide)
  - 73% patients had prior exposure to autologous stem cell transplant
- 3 patients were lenalidomide refractory (according to IMWG criteria)

PI = proteasome inhibitor; IMiD = Immunomodulatory drug; IMWG: International Myeloma Working Group; MM: multiple myeloma;

Maximum % Change in M Protein from Baseline

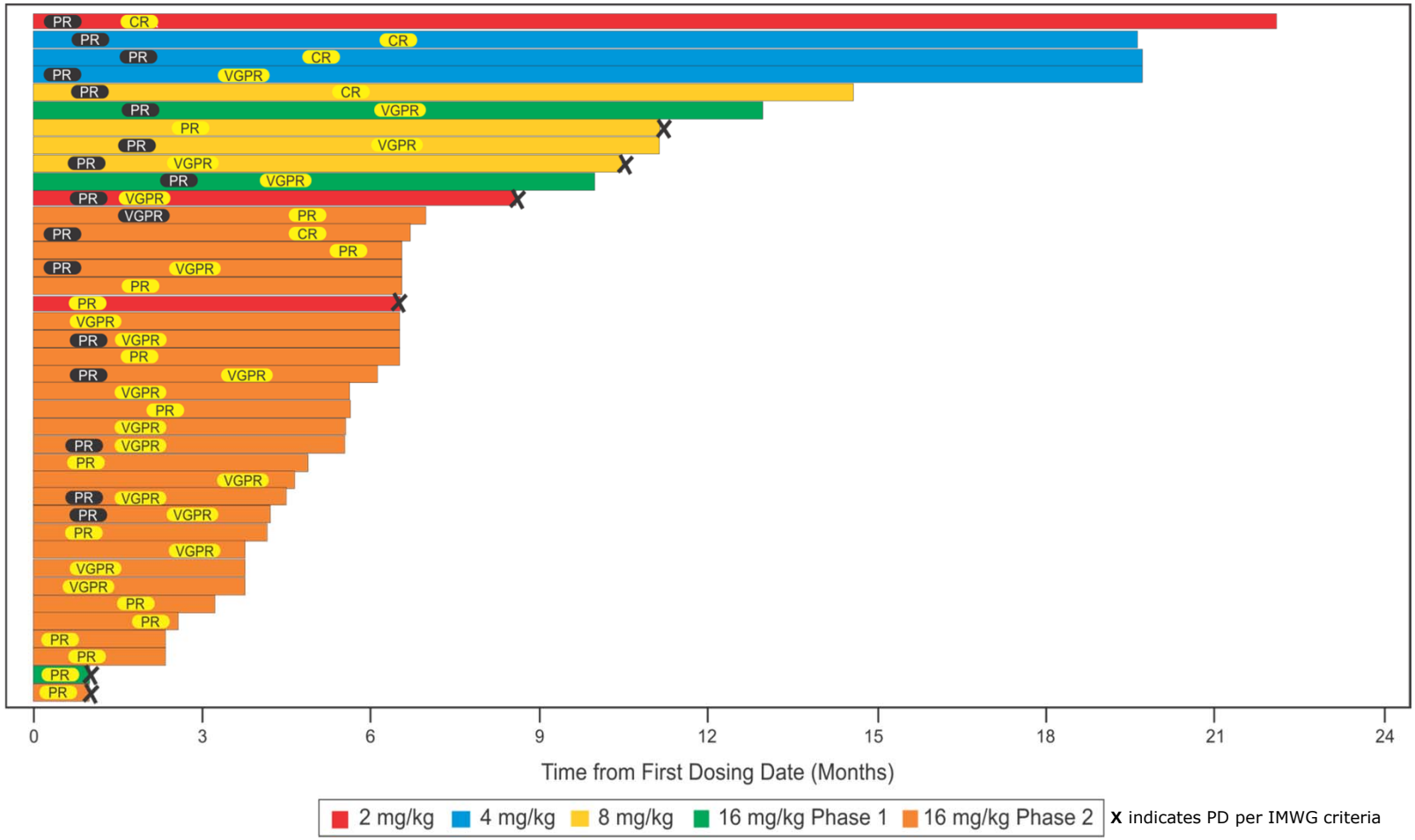
Part 1
Dose Escalation Study
2-, 4-, 8- & 16 mg/kg dose
N=13

Part 2
Expansion Cohort Study
16 mg/kg dose
N=30



- Majority had >50% reduction of M protein

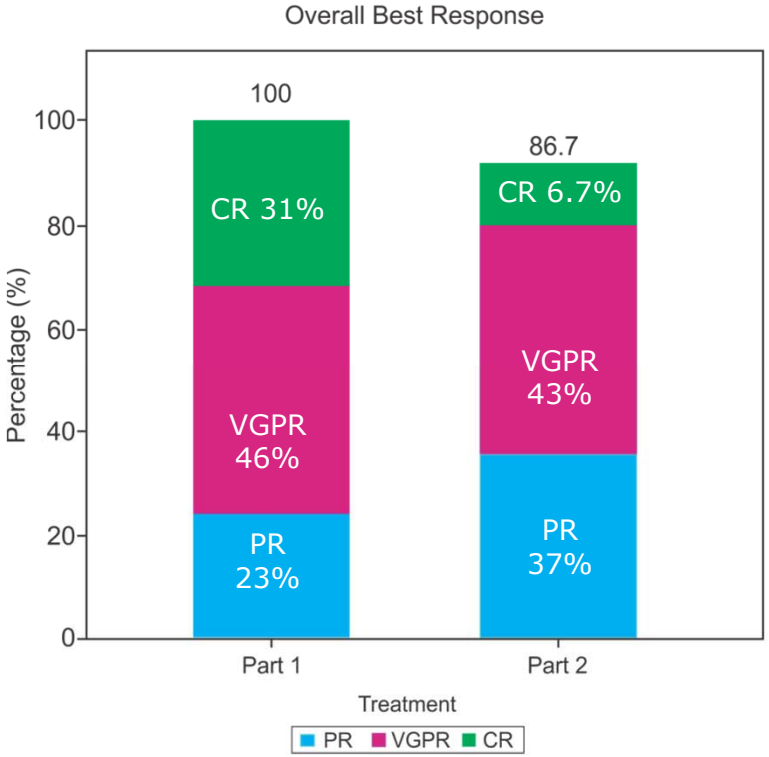
Best Response (PR or Better) and Duration of Follow-up

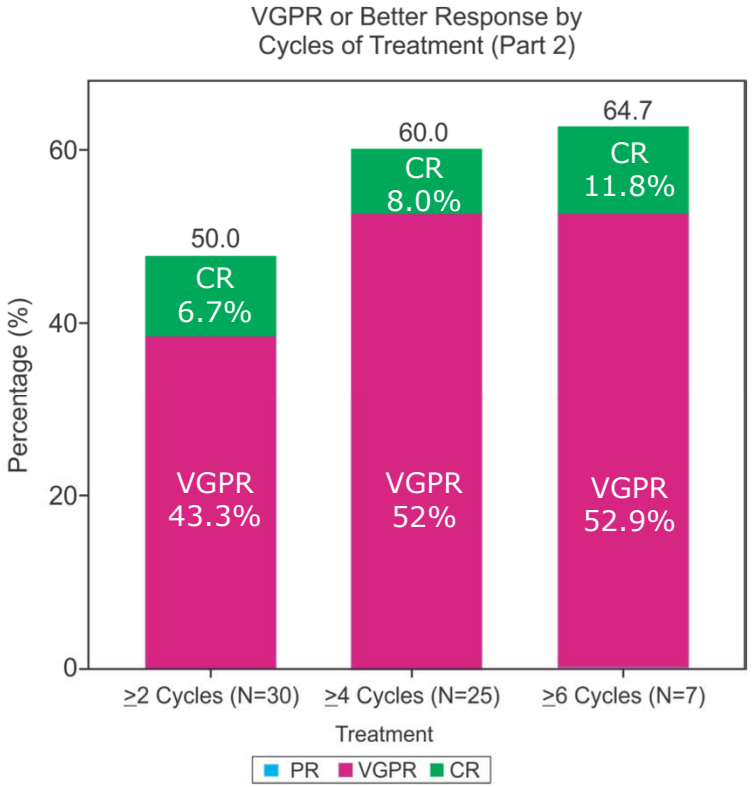


- VGPR or better was 75% in patients who were treated for at least 6 months.

CR: complete response; PR: partial response; VGPR: very good partial response

Overall Best Response





- Mean duration of follow-up: 12.9 months (Part 1, range: 4.0-22.1) & 5.6 months (Part 2, range: 2.7 – 7.0)
- Median time to response: 1 month for 16 mg/kg in part 2
- Median time to CR in part 2 was 4.9 months
- As has been observed with other mAbs, DARA may interfere with IFE
  - Interference assay to be validated

CR: complete response; PR: partial response; VGPR: very good partial response.

Safety

- Safety data collected from 45 patients
- No DLTs were reported
- Part 1: 4 patients discontinued treatment:
  - 3 disease progression (1 each in 2-, 8- and 16-mg/kg dose cohort)
  - 1 AE (2-mg/kg dose cohort, cardiac disorder due to recurrence of low grade QT prolongation), unrelated to DARA
- Part 2: 1 patient discontinued due to IRR (laryngeal edema)

AE: adverse event; DARA: daratumumab; DLT: dose limiting toxicity; IRR, infusion related reaction.

Most Common (Incidence in >10% Patients) Adverse Events

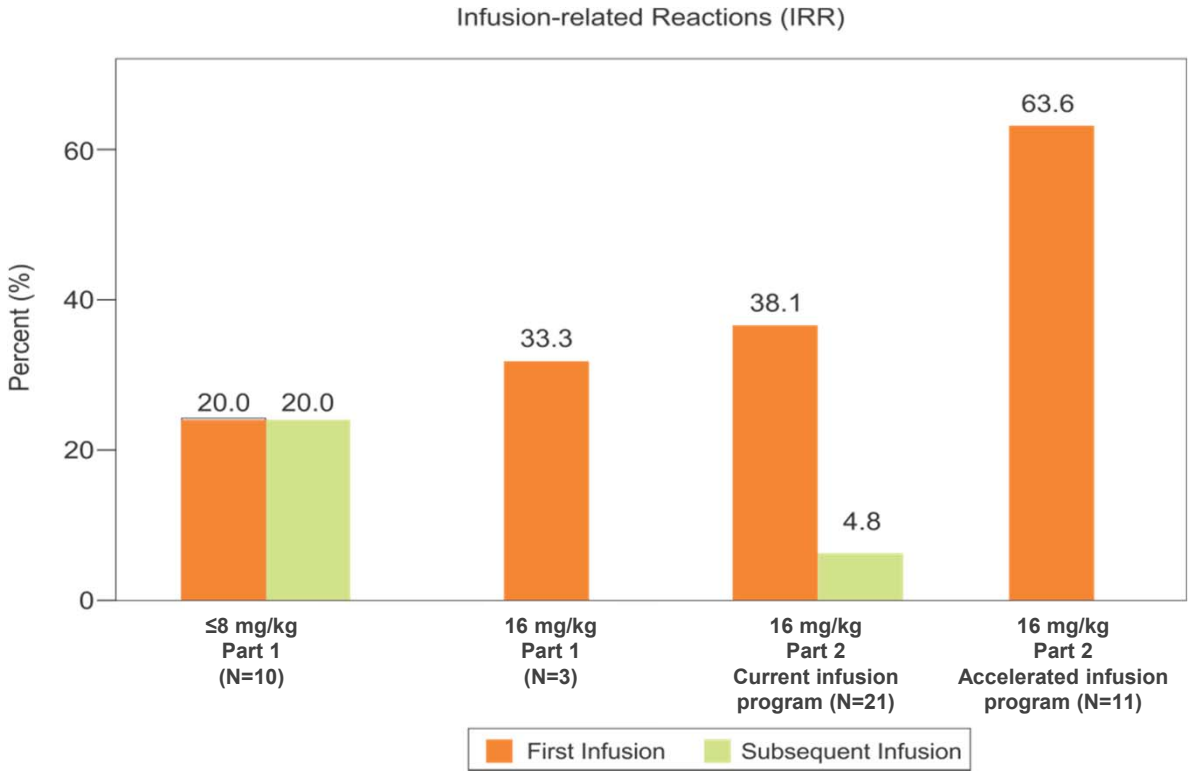
	Part 1 N=13	Part 2 N=32	Total N=45
Total number of patients with AEs, %	100	100	100
Neutropenia	62	65	64
Muscle Spasms	62	38	44
Diarrhea	54	18	31
Fatigue	62	16	29
Cough	31	28	29
Constipation	54	13	27
Nausea	38	19	24
Nasopharyngitis	62	3	20
Bone Pain	31	13	18
Upper Respiratory Tract Infection	46	3	16
Insomnia	31	6	16
Dyspnea	23	6	11
Anemia	31	19	11

AE: adverse event.

Daratumumab Infusions

	16 mg/kg	
	Current infusion program N=21	Accelerated infusion program N=11
Total number of full infusions per patient, Mean (SD)	15.6 (2.77)	10.5 (4.06)
Median duration of first infusion (hours)	8.0	5.4
Median duration of second infusion (hours)	6.5	4.3
Median duration of subsequent infusions (hours)	5.5	3.6

Infusion-related Reactions



- **Majority grade 1 and 2**
- 19/45 patients reported infusion-related reactions
- Most infusion-related reactions (86%) occurred during first infusion
- 18/19 patients with infusion-related reactions recovered and were able to continue the subsequent infusion

Serious Adverse Events

- 15 SAEs reported:
  - Part 1: 7, all assessed as unrelated to DARA
  - Part 2: 8, 4 were DARA-related

- DARA related SAEs:
  - Pneumonia, neutropenia, diarrhea (1 patient each receiving 16 mg/kg, early infusion program)
  - Laryngeal edema (1 patient receiving 16 mg/kg, accelerated infusion program)

DARA: daratumumab; SAE: serious adverse events

Conclusions (1)

- ORR was 100% in part 1 (31% CR, 46% VGPR), and 87% in part 2 (7% CR, 43% VGPR)
  - VGPR or better was 75% in patients treated for at least 6 months
- Data from part 1 are mature and show impressive CR rates
- Early results from part 2 are consistent with part 1
  - Median follow-up <6 months with depth of response expected to further improve

CR: complete response; ORR: overall response rate; VGPR: very good partial response

Conclusions (2)

- Accelerated infusion was tolerable but associated with higher incidence of grade 1/2 AEs
  - Accelerated infusion will require further investigation
- DARA+LEN/DEX treatment demonstrated a favorable safety profile with manageable toxicities in relapsed and RR MM patients
- Phase 3 clinical development of DARA in combination with LEN/DEX is ongoing
  - MMY3003-POLLUX (relapsed/refractory), enrolling
  - MMY3008-MAIA (frontline), enrollment expected to start early 2015

AE: adverse event; DARA: daratumumab; DEX: dexamethasone; LEN: lenalidomide; MM: multiple myeloma; RR: relapsed refractory

Acknowledgements

- We thank the patients, their carers and investigators who participated in this study

An Open-label, Multicenter, Phase 1b Study of Daratumumab in Combination with Backbone Regimens in Patients with Multiple Myeloma

Philippe Moreau, MD; Maria-Victoria Mateos, MD, PhD; Joan Bladé,MD; Lotfi Benboubker, MD; Javier de la Rubia, MD, PhD; Thierry Facon, MD; Raymond Comenzo, MD; Joseph Fay, MD; Xiang Qin, MS; Tara Masterson, MS; Jordan Schecter, MD; Tahamtan Ahmadi, MD, PhD; Jesus San-Miguel, MD, PhD

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MMY1001: Objective

- The aim of this ongoing open-label, 4-arm, multicenter, phase 1b study was to
  - Evaluate the safety and tolerability of daratumumab, at a starting dose of 16 mg/kg, in combination with other MM backbone treatments, including
    - Bortezomib (sc)-dexamethasone (VD)
    - Bortezomib (sc)-thalidomide-dexamethasone (VTD)
    - Bortezomib (sc)-melphalan-prednisone (VMP)
    - Pomalidomide-dexamethasone (POM-D)

sc, subcutaneous.

MMY1001: Demographics, exposure, and disposition

	VD + DARA (n = 6)	VMP + DARA (n = 6)	VTD + DARA (n = 6)	POM-D + DARA (n = 7[a])
Median age (range), y	72.5 (50-82)	72 (67-75)	57 (40-61)	62 (45-85)
Sex				
Male	2	3	2	4
Female	4	3	4	3
Median # daratumumab infusions (range)	9 (8-11)	12.5 (10-14)	8 (7-11)	11 (1-17)
Median # cycles	5	4	4	4
Disposition	1 subject electively taken off study for ASCT after cycle 4	No discontinuations	5 subjects electively taken off study for ASCT after cycle 4	3 subjects discontinued study (1 due to physician decision after 1st dose; 2 due to PD)

V, bortezomib; D, dexamethasone; DARA, daratumumab; M, melphalan; P, prednisone; T, thalidomide; POM, pomalidomide; ASCT, autologous stem cell transplant; PD, progressive disease.

[a]2 refractory to PI; 1 refractory to IMID; 3 refractory to both PI/IMID; 1 subject relapsed but not refractory; 4 refractory to the last line of prior therapy.

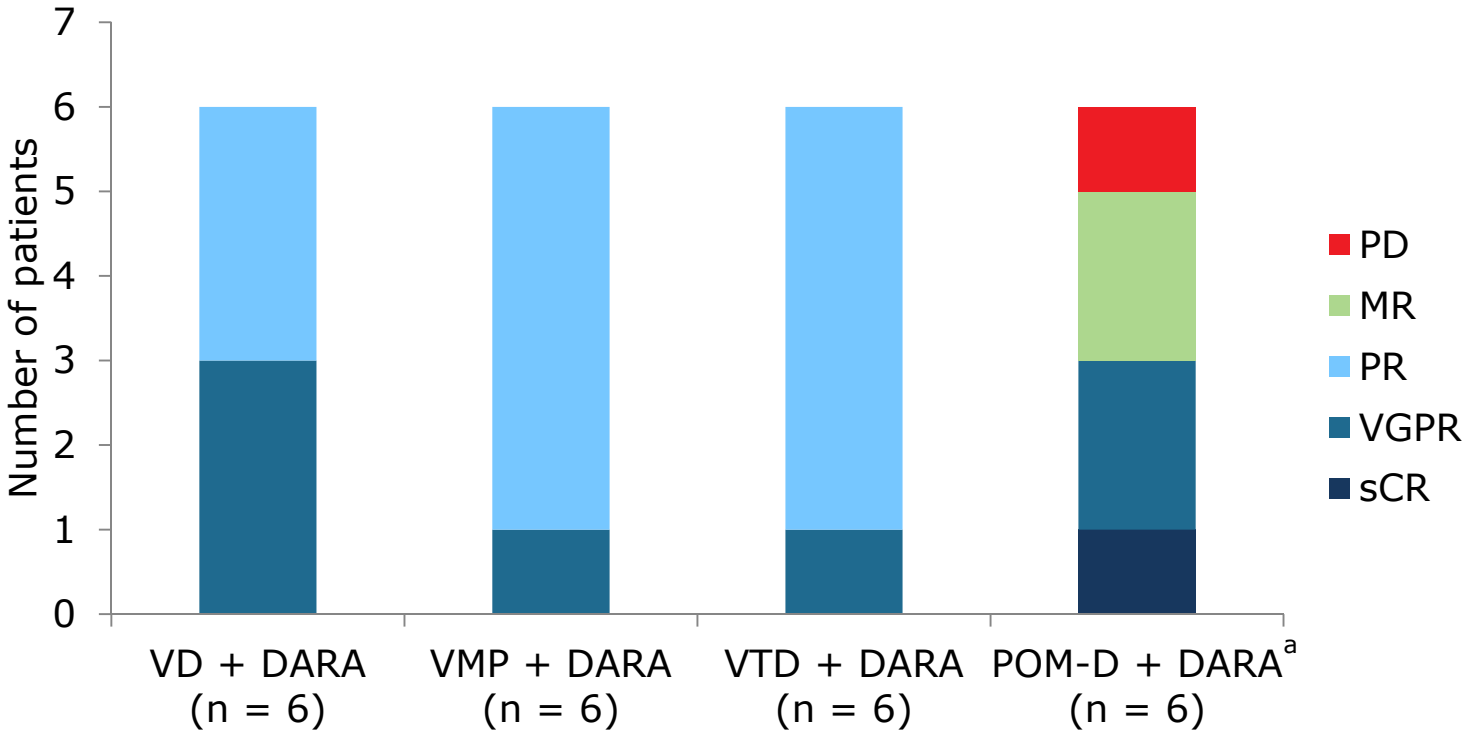
All patients treated with DARA 16 mg/kg.

MMY1001: Safety

	VD + DARA (n = 6)	VMP + DARA (n = 6)	VTD + DARA (n = 6)	POM-D+ DARA (n = 7)
Serious AEs	• Pneumonia[a,b] • Soft tissue infection[a,b] • Dehydration[a,b] • Positive indirect Coombs assay[c]	None	None	• Infectious pneumonia[c]
Grade ≥3 AEs (all Gr. 3 except for Gr. 4 neutro-penia in POM-D)	• Neutropenia[b,c] • Anemia[b,d]	• Neutropenia (n = 2)[a] • Thrombocytopenia[c]	• Neutropenia[b,c] • Anemia[b,d]	• Neutropenia (n = 5) • Anemia (n = 2) • Thrombocytopenia • Leukopenia • 1 episode each of diarrhea, flank pain, peripheral sensory neuropathy, hypokalemia, pneumonia, hip fracture, rash, eye hemorrhage, and decreased lymphocyte count
Infusion related reactions	All Grade 1 or 2			

V, bortezomib; D, dexamethasone; DARA, daratumumab; M, melphalan; P, prednisone; T, thalidomide; POM, pomalidomide; AE, adverse events; Gr, grade.
[a]Not related to daratumumab, [b]same subject, [c]possibly or probably related to daratumumab, [d]reported pre-dose.
Each AE occurred in 1 subject unless otherwise noted.
All patients treated with DARA 16 mg/kg.

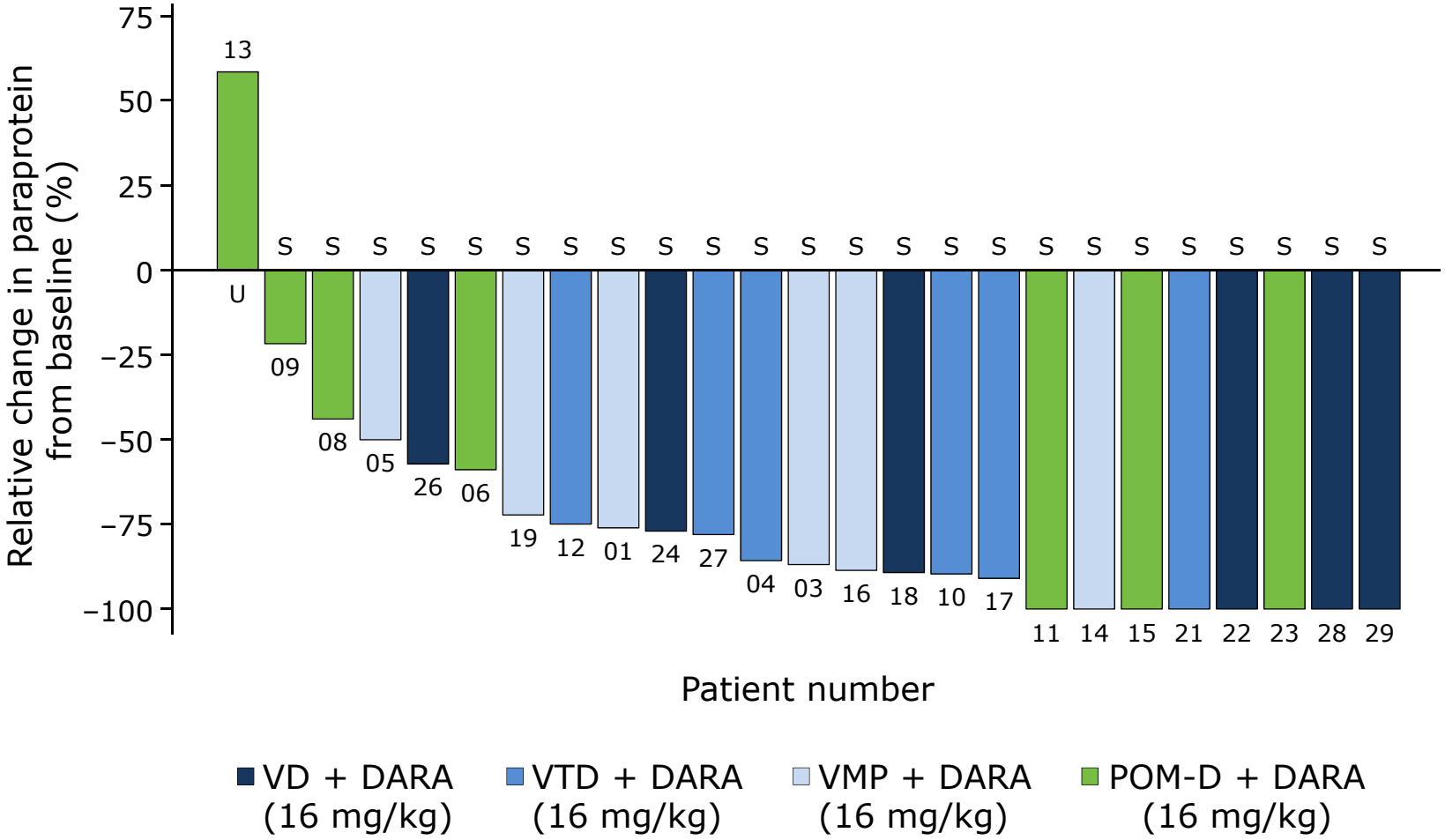
MMY1001: Efficacy



- ORR:
  - 100% in newly diagnosed group
  - 50% in the relapsed group

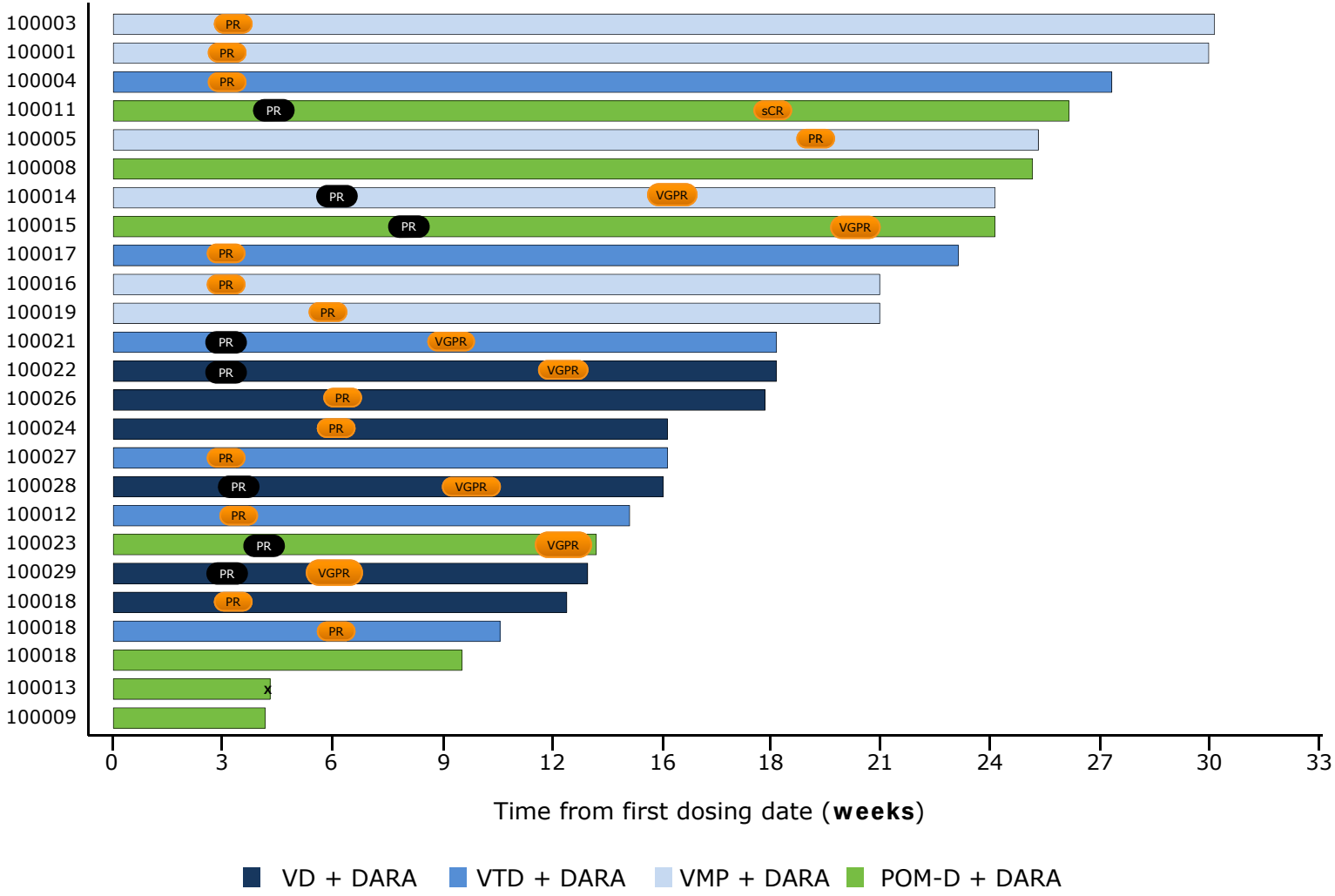
V, bortezomib; D, dexamethasone; DARA, daratumumab; M, melphalan; P, prednisone; T, thalidomide; POM, pomalidomide.
sCR, stringent complete response; VGPR, very good partial response; PR, partial response; MR, minimal response; PD, progressive disease.
[a]1 VGPR confirmed, 1 VGPR repeat assessment pending.
All patients treated with DARA 16 mg/kg.

MMY1001: Maximal percentage change in paraprotein from baseline



V, bortezomib; D, dexamethasone; DARA, daratumumab; M, melphalan; P, prednisone; T, thalidomide; POM, pomalidomide.

MMY1001: Best response (PR or better) and duration of follow up



sCR, stringent complete response; VGPR, very good partial response; PR, partial response.
V, bortezomib; D, dexamethasone; DARA, daratumumab; M, melphalan; P, prednisone; T, thalidomide; POM, pomalidomide.
All patients treated with DARA 16 mg/kg.

MMY1001: Summary

- Addition of 16 mg/kg daratumumab to the various backbones was well tolerated in all evaluable patients and did not result in significant additional toxicity
- Daratumumab was associated with promising response rates in combination with VD, VMP, VTD and POM-D
- Daratumumab does not appear to have a negative impact on stem cell mobilization
- Phase 3 studies are either ongoing or will be initiated shortly
  - VD (relapsed, MMY3004-CASTOR)
  - VMP (non-transplant eligible, MMY3007-ALCYONE)
  - VTD (induction, MMY3006/IFM-HOVON-CASSIOPEIA)

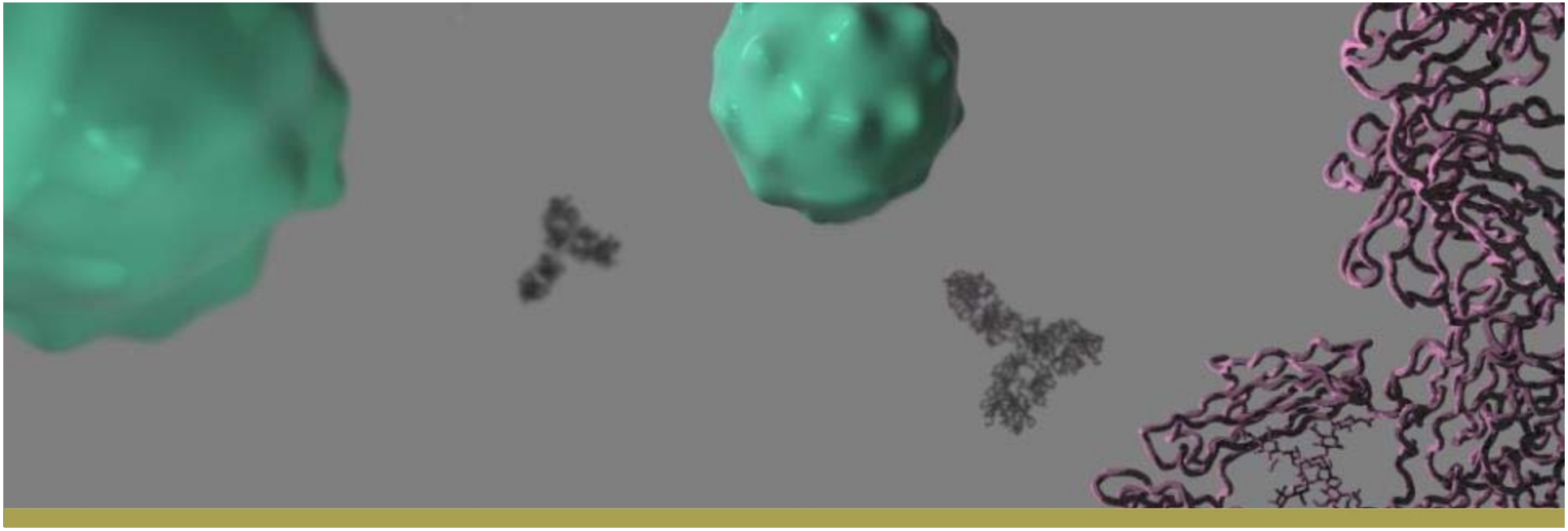
V, bortezomib; D, dexamethasone; M, melphalan; P, prednisone; T, thalidomide; POM, pomalidomide.

MMY1001 (NCT01998971): Phase Ib study of daratumumab + backbone treatments

- VD: bortezomib (1.3 mg/m^2 twice weekly x 4 cycles, then once weekly x 14 cycles)/dexamethasone (20 mg)[a]
  - Newly diagnosed; n = 6
- VMP: bortezomib (1.3 mg/m^2 twice weekly x 1 cycle, then once weekly x 8 cycles)/melphalan (9 mg/m^2)/prednisone (60 mg/m^2)[b]
  - Newly diagnosed, transplant ineligible; n = 12
- VTD: bortezomib (1.3 mg/m^2 twice weekly x 4 cycles, then once weekly x 14 cycles)/thalidomide (100 mg daily x 21 days)/dexamethasone (20 mg)[a]
  - Newly diagnosed; n = 12
- POM-D: pomalidomide (4 mg once daily)/dexamethasone (40 mg)[c]
  - Relapsed/refractory, ≥2 lines of therapy, including 2 consecutive cycles of lenalidomide and bortezomib; n = 50 subjects maximum

[a]Daratumumab once weekly x 2 cycles, then once every 3 weeks x 16 cycles or until transplantation.
[b]Daratumumab once weekly x 1 cycle, then every 3 weeks x 8 cycles.
[c]Daratumumab once weekly x 2 cycles, then once every 2 weeks x 4 cycles, then once every 4 weeks x 7 cycles or until disease progression; dexamethasone 20 mg if age >75 y.

ClinicalTrials.gov Identifier: NCT01998971. Available at: http://www.clinicaltrials.gov/ct2/show/NCT01998971?term=NCT01998971&rank=1. Accessed 10/27/14.



The Future of Treatment of Multiple Myeloma

Presented by Prof. Antonio Palumbo
University of Torino

Genmab

A new treatment paradigm for MM

Take home messages

Antonio Palumbo MD
Professor of Hematology
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University of Torino, Torino, Italy

EMN
Trialist Group

Disclosures for Antonio Palumbo, MD

Research Support/P.I.	No relevant conflicts of interest to declare
Employee	No relevant conflicts of interest to declare
Consultant	Amgen, Bristol-Myers Squibb, Genmab A/S, Celgene, Janssen-Cilag, Millennium Pharmaceuticals Inc., Onyx Pharmaceuticals
Major Stockholder	No relevant conflicts of interest to declare
Speakers Bureau	No relevant conflicts of interest to declare
Honoraria	Amgen, Array BioPharma, Bristol-Myers Squibb, Genmab A/S, Celgene, Janssen-Cilag, Millennium Pharmaceuticals Inc., Onyx Pharmaceuticals, Sanofi Aventis
Scientific Advisory Board	No relevant conflicts of interest to declare

Presentation includes discussion of the off-label use of a drug or drugs

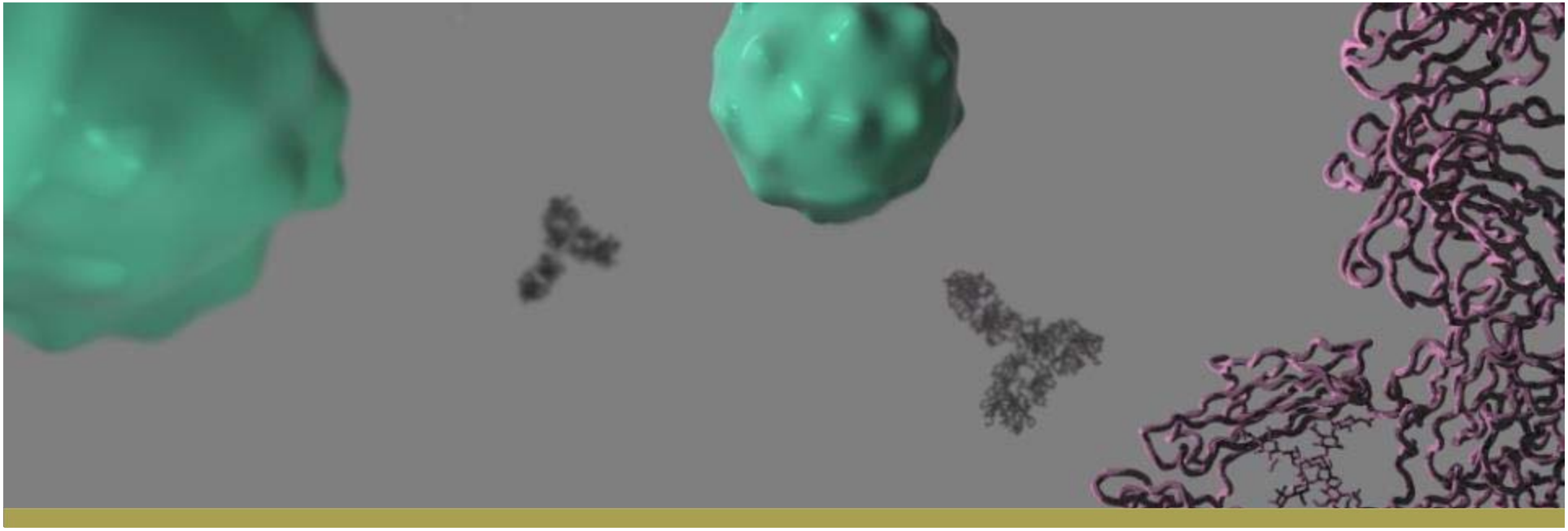
A new treatment paradigm for MM

TAKE HOME MESSAGES

- CD38 will change treatment paradigm in MM
- CD38 will become the backbone of MM therapy

- Which combinations and treatment schedule are current questions
- Combo will include IMiDs and PIs or other agents

- CD38 will improve MM outcome
- CD38 will induce MM cure



Daratumumab

Presented by Jan van de Winkel

CEO, Genmab

Genmab

CD38 Landscape: Direct In-House Pre-Clinical Comparison with Surrogates of Competitor Antibodies

		Daratumumab (Genmab)	MOR202 [1] (MorphoSys)	SAR 650984 [1, 2] (Sanofi-Aventis)	AB79 (Millennium/Takeda)
	Origin	Human	Human	Humanized	Human
	Development phase	Phase III	Phase I/IIa	Phase I/II	Pre-clinical
	Binding [3]	+++	++	+++	+++
Mechanism of Action	ADCC (max lysis) [3]	++	++	++	++
	CDC (max lysis) [3]	+++	+	+	++
	Phagocytosis [3, 4]	+++	++	nd	+++
	Ecto-enzyme function	+	-	+++	+
	Direct PCD [5, 6]	-	-	++	-
	PCD after cross-linking [5, 6]	+++	+++	+++	+++

*MOR202 clone MOR03087; [1]:surrogate mAb produced in HEK cells, generated using VH and VL sequences as published in PCT applications WO2012/041800 (MOR03087) and WO2008/047242 (38SB19); [2]:38SB19; [3]:Daudi cells; [4]:based on EC50 data, [5]:Ramos cells [6]: PCD: Programmed cell death, measured by Annexin V positivity and caspase-3 activation. nd = not determined

Expansive Daratumumab Development

12 Ongoing or Announced Studies

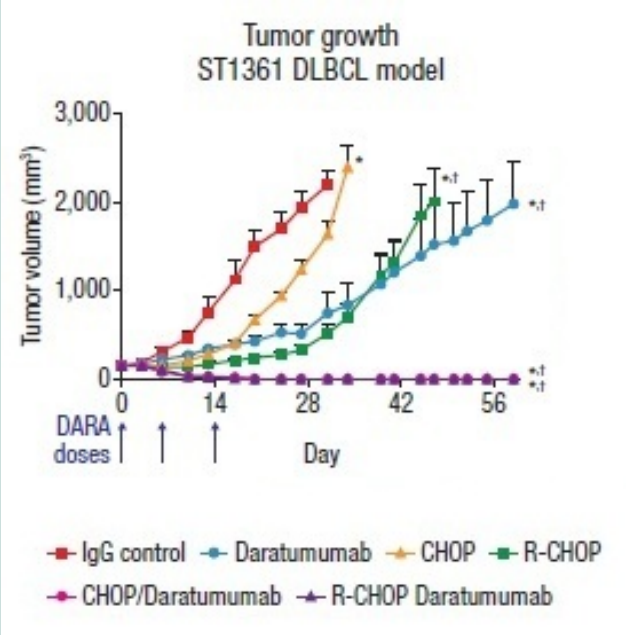
Indication	Disease Stage	Therapy	Development Phase (Pre-clinical / I / I/II / II / III / IV)
Multiple Myeloma	Smoldering	Mono	
	Front line (transplant & non-transplant)	Dara + VMP*	
		Dara + Revlimid + Dex*	
		Dara + VTD*	
		Multi combo: 1 Study	
	Relapsed or Refractory	Dara + Revlimid + Dex 2 Studies	
		Dara + Velcade + Dex 1 Study	
		Mono, Japan	
		Mono, safety	
	Double Refractory	Mono, BTD population	
	Maintenance		Integrated into some study protocols
NHL	Relapsed or Refractory	Mono	
Non-MM	Various	Potential in: ALL, AML, Plasma Cell Leukemia, CLL, Mantle Cell Lymphoma, DLBCL, FL	

*PhIII announced, not yet started.

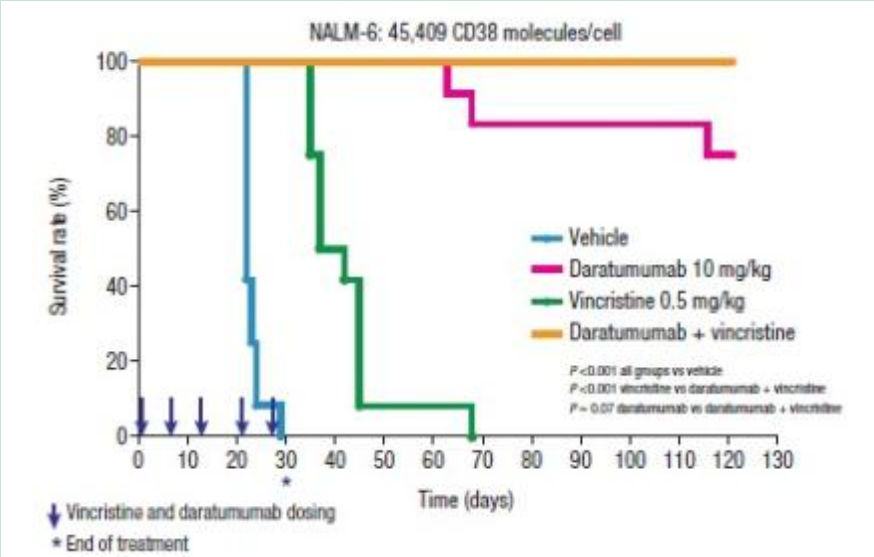
Daratumumab Beyond Multiple Myeloma

Pre-clinical Activity in DLBCL & ALL (EHA 2014)

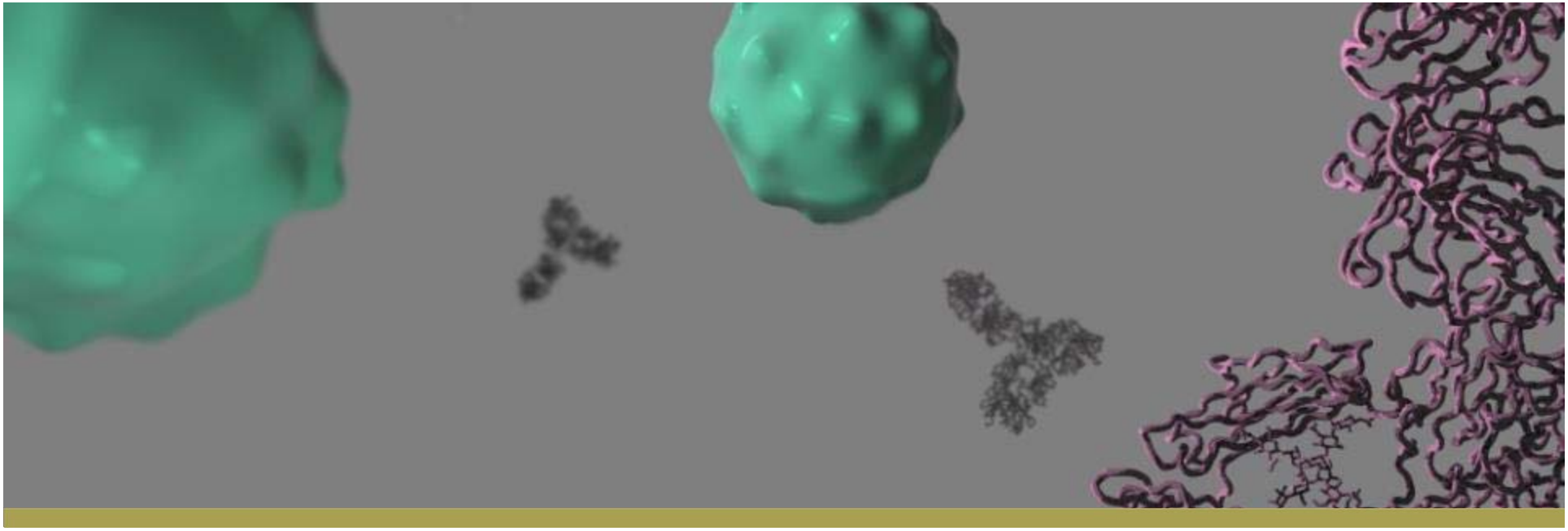
Effect daratumumab on tumor growth in patient-derived DLBCL model



Effect daratumumab with or without vincristine in ALL xenograft model



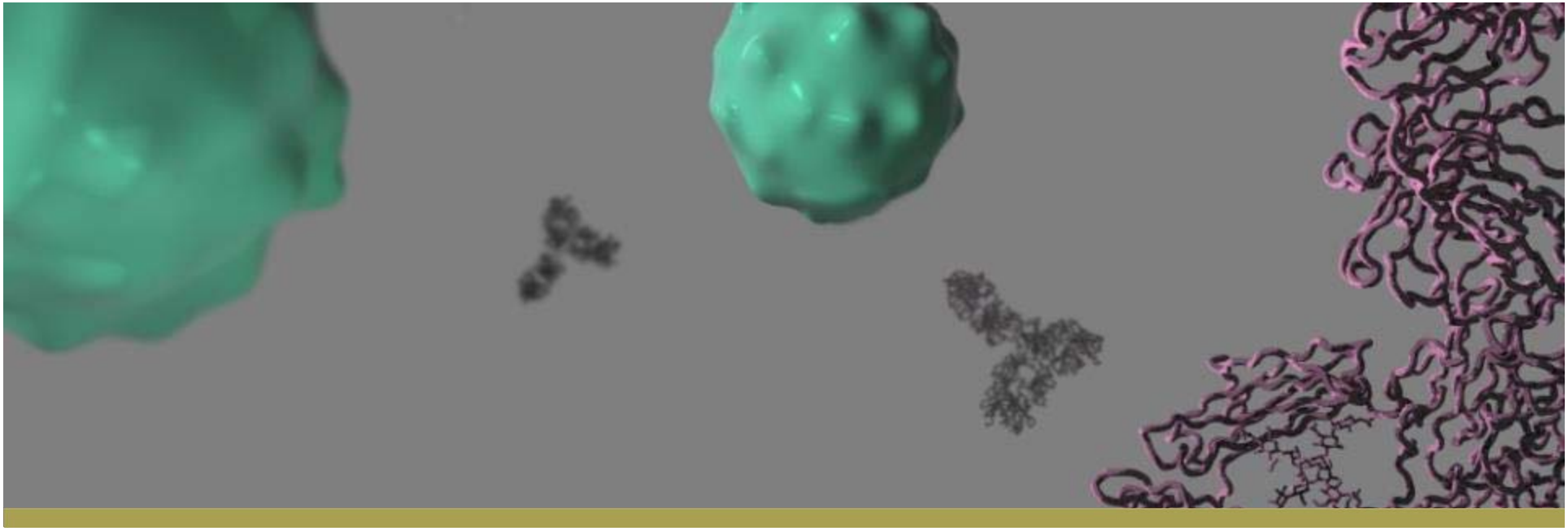
Data presented at EHA 2014



Daratumumab Q&A

Dr. Paul Richardson, *Dana Farber Cancer Institute*; Prof. Torben Plesner, *Vejle Hospital*; Prof. Antonio Palumbo, *University of Torino*; Steen Lisby & Jan van de Winkel, *Genmab*

Genmab



News from the Clinic

Ofatumumab

Presented by Prof. Marinus van Oers

Academic Medical Center

Genmab

Ofatumumab (OFA) Maintenance Prolongs PFS in Relapsed CLL: Interim Analysis Results of the phase III PROLONG Study

(OMB112517/HOVON 101 study)

Abstract 21

Marinus van Oers, Kazimierz Kuliczkowski, Lukas Smolej, Mario Petrini, Fritz Offner, Sebastian Grosicki, Mark-David Levin, Ira Gupta, Jennifer Phillips, Vanessa Williams, Steen Lisby, and Christian Geisler, on behalf of the PROLONG Study Investigators

HOVON

gsk GlaxoSmithKline

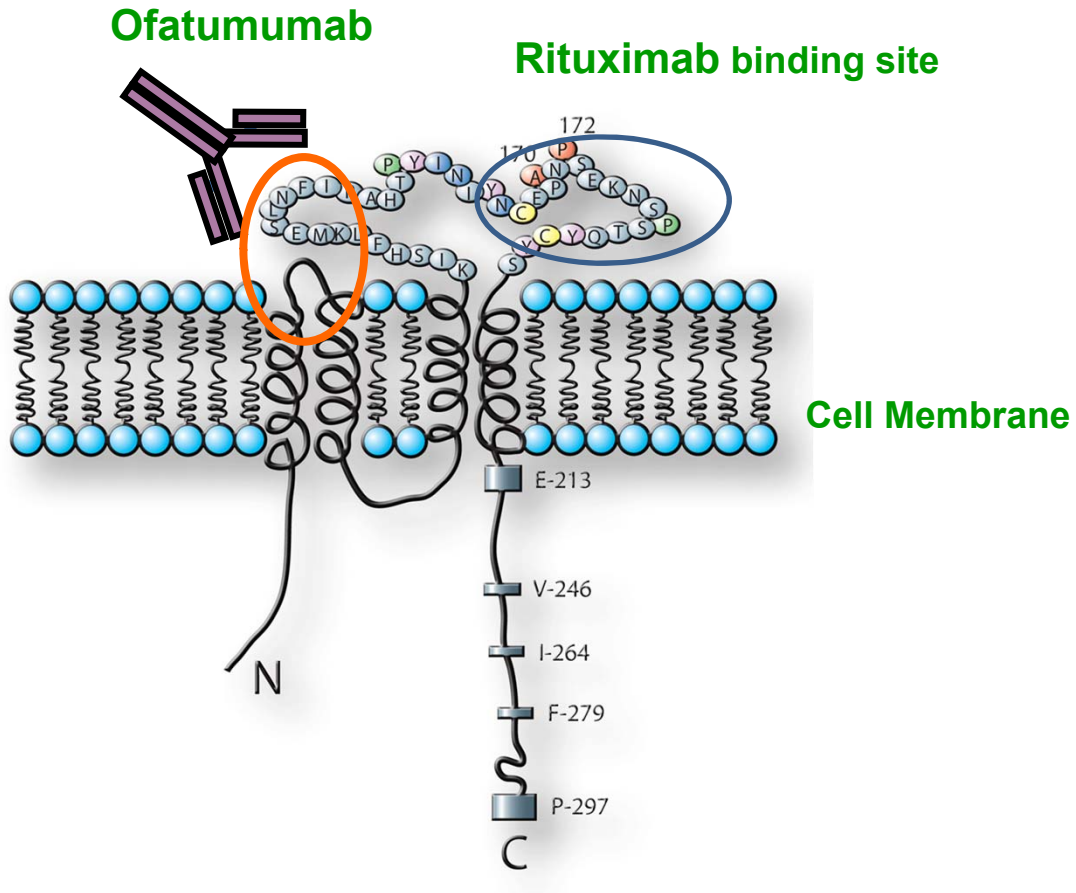
PROLONG study: Rationale

- Still no curative treatment for CLL
- Decreasing response duration with subsequent lines of therapy
- Similarities in biological behavior between CLL and Follicular Lymphoma (FL)
- There is a role for maintenance in FL
- There is interest in safe and effective maintenance treatment in CLL

PROLONG study: Objectives

- Primary
  - Evaluate PFS with ofatumumab maintenance treatment vs. observation after remission induction in relapsed CLL
- Secondary
  - To evaluate safety, tolerability and quality of life
  - To evaluate ofatumumab pharmacokinetics in patients on ofatumumab maintenance

Ofatumumab: a human type I CD20 Mab (IgG1κ)



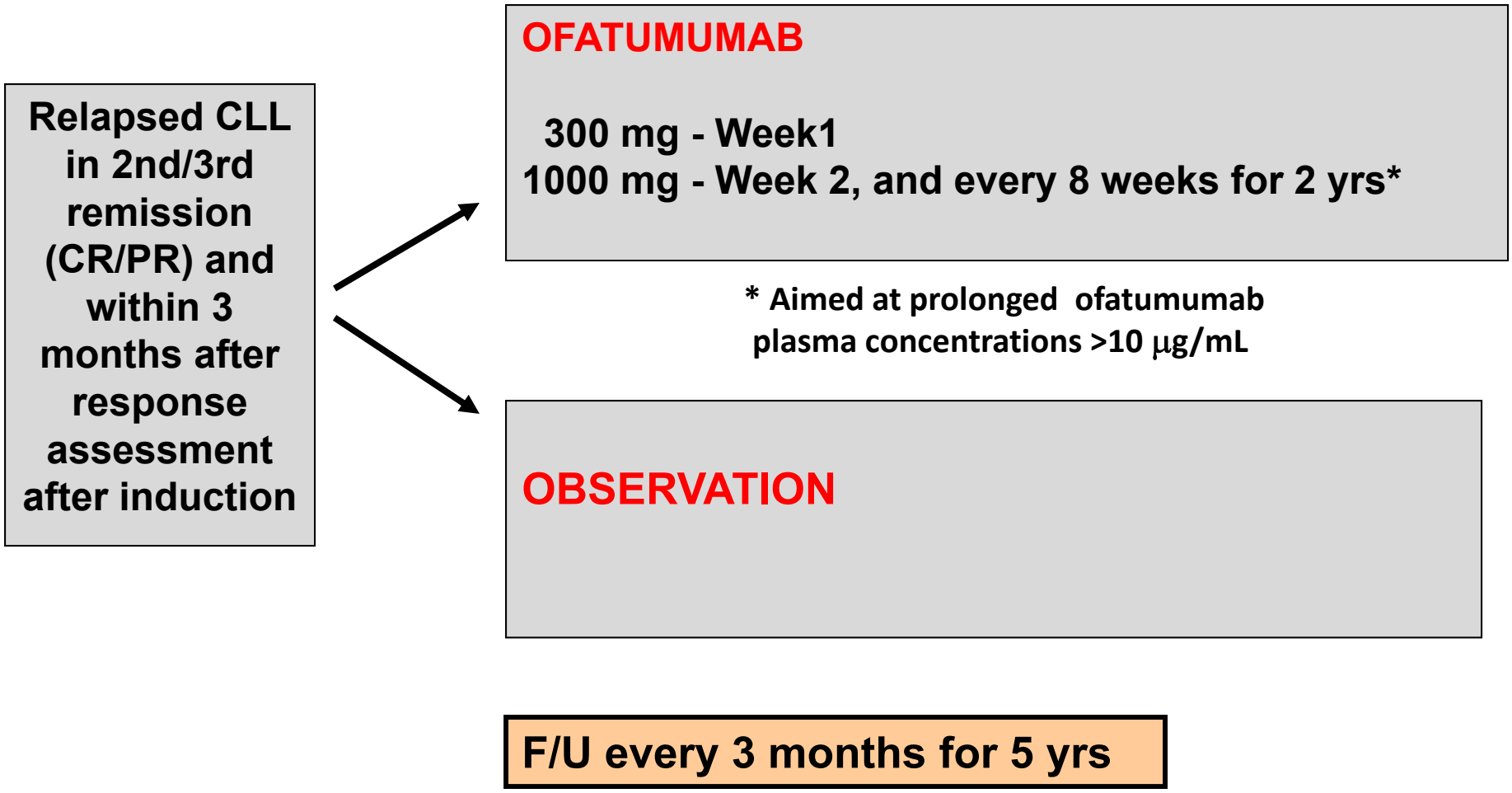
- Potent CDC activity, also in rituximab-resistant cells[1,2,3]
- More potent ADCC than rituximab[4]
- Active in rituximab refractory CLL[5]

ADCC = antibody-dependent cell-mediated cytotoxicity; CDC = complement-dependent cytotoxicity

1. Teeling, *J Immunol* 2006; 177:36
2. Teeling, *Blood* 2004; 104:1793
3. Barth, *Br J Heam* 2012; 156:490
4. Craigen, ASH 2009 Abstract 1725
5. Wierda, *Blood* 2011; 118: 5126

Epitope mapping image: www.pepscan.com/presto/products-services/epitope-mapping; Cell image :DAVA Oncology;

PROLONG study: Design



PROLONG study: Stratifications and Interim Analysis

- Stratification at randomization
  - Number of previous re-induction regimens (1 or 2)
  - CR/PR at study entry
  - Immunochemotherapy Y/N
  - ONLY Alkylator monotherapy Y/N

- Planned interim analysis by independent DSMB for toxicity (infections) and efficacy- at 2/3 of total number of events (187 events)
  - 474 patients
  - Median follow-up: 19.1 months
  - At time of interim analysis 25% of patients had received all 13 cycles of Ofatumumab

PROLONG study: Key Inclusion/Exclusion Criteria

Inclusion

- CLL according to revised NCI-WG CLL criteria
- Age above 18 years
- WHO performance status 0-2
- CR/ PR within 3 months of response assessment after the last dose of $2^{nd}/3^{rd}$ line treatment

Exclusion

- Refractory disease
- Prior maintenance
- Active AIHA requiring treatment
- Prior stem cell transplantation
- Chronic or active infection requiring treatment
- Screening labs
  - Neutrophils <1.0 x 10^9/L; Platelets <50 x 10^9/L; Creatinine>1.5 X ULN; Total bilirubin, ALT, AST>2.5 x ULN

PROLONG study: Endpoints

- PFS, defined as the time from randomization to the date of disease progression or death due to any cause.

- Secondary Endpoints:
  - TTNT/OS
  - Safety and Tolerability
  - Health-related Quality of Life
  - PK

Baseline Patient Characteristics (n=474)

	OFA (n=238)	Obs (n=236)
Age, Years, median (range)	64 (33-86)	65 (39-87)
<70, %	71	69
≥ 70, %	29	31
Male, %	68	67
Time since diagnosis , median (years)	6.0	5.0
Response to last CLL treatment, n (%)		
CR	41 (17)	42 (18)
CRi	4 (2)	4 (2)
PR	193 (81)	189 (80)
Missing	0	1 (<1)
No. of prior treatment, n (%)		
2	168 (71)	166 (70)
3	66 (28)	62 (26)
Other	4 (2)	8 (3)
Type of prior treatment, n (%)		
Alkylator Only	14 (6)	9 (4)
Chemoimmunotherapy	191 (80)	189 (80)
Other	33 (14)	38 (16)

Baseline Prognostic Factors (n=474)

	OFA (n=238)	Obs (n=236)
Baseline MRD, n (%)		
Negative	**31 (13)**	**41 (17)**
Positive	**137 (58)**	**107 (45)**
Missing	**70 (29)**	**88 (37)**
Cytogenetics, n (%)		
11q-	**15 (6)**	**12 (5)**
17p-	**7 (3)**	**4 (2)**
6q- or +12 or 13q-	**44 (18)**	**16 (7)**
No aberration	**150 (63)**	**171 (72)**
Missing	**22 (9)**	**33 (14)**
B_2 **Microglobulin,** n (%)		
≤3500 μg/L	**157(66)**	**163 (69)**
>3500 μg/L	**79 (33)**	**68 (29)**
Missing	**2 (<1)**	**5 (2)**
IgVH mutational status, n (%)		
Mutated	**47 (20)**	**66 (28)**
Unmutated	**129(54)**	**108 (46)**
Not available	**3 (1)**	**1 (<1)**
Missing	**59 (25)**	**61 (26)**

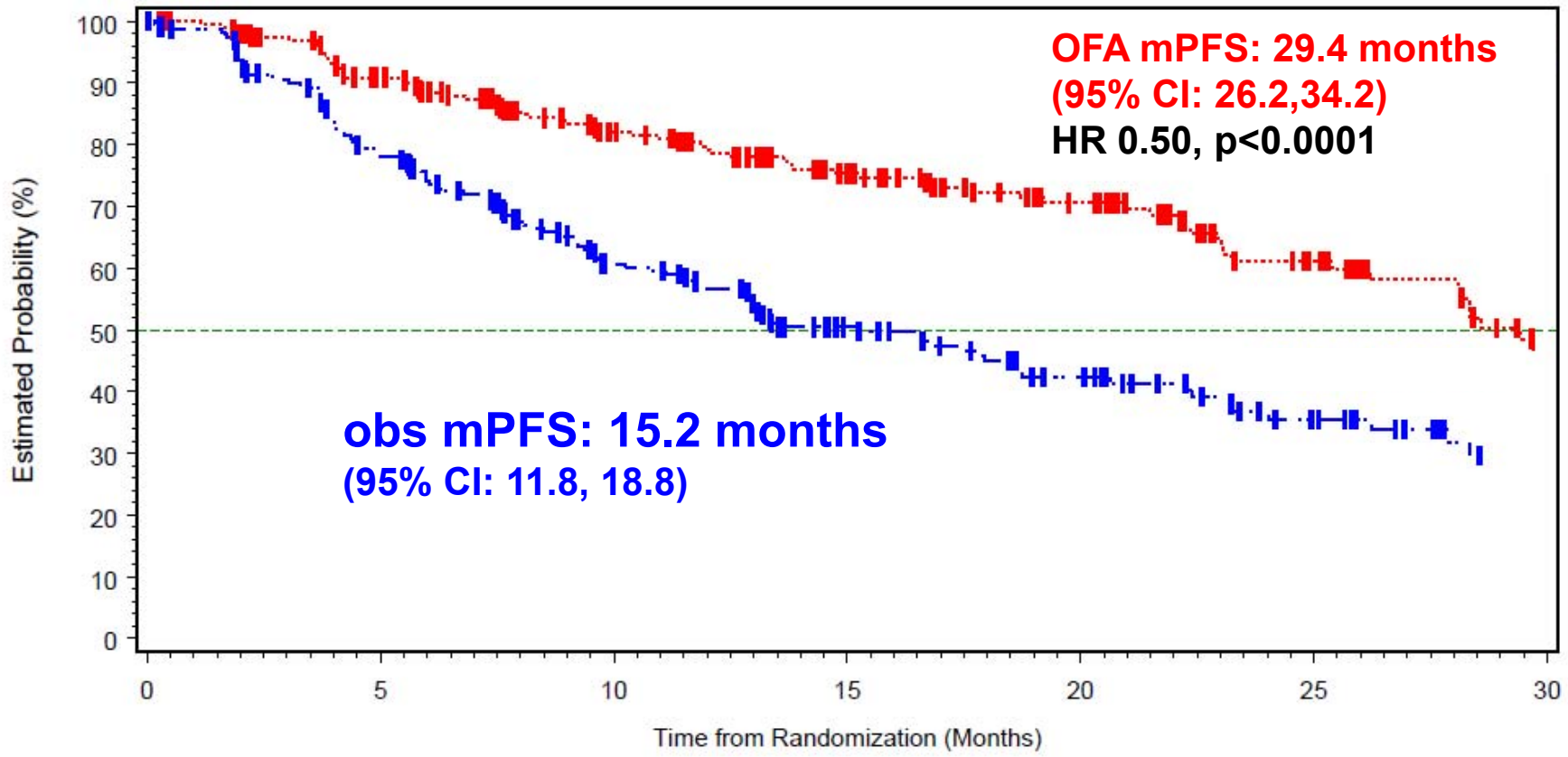
Adverse Event Overview

Number of patients with AE, n (%)	OFA (n=237)	Obs (n=237)
AEs, any	205 (86)	170 (72) **
AEs related to study treatment	142 (60)	NA
AEs leading to withdrawal from study	0	0
AEs ≥ Grade 3	108 (46)	67 (28)
Neutropenia	56 (24)	23 (10) **
Infections	30 (13)	20 (8) NS
Thrombocytopenia	4 (2)	8 (3)
Infusion-related reactions (IRR)	3 (1)	NA
Death (n)	2 (<1)	5 (2)
Infections/sepsis	1 (<1)	0
Progressive disease	0	1 (<1)
Secondary malignancy	0	0
Other	1 (<1)	4 (2)

** P< 0.0001 Cochran-Mantel-Haenszel adjusting for stratification factors

PROLONG: Progression-free Survival

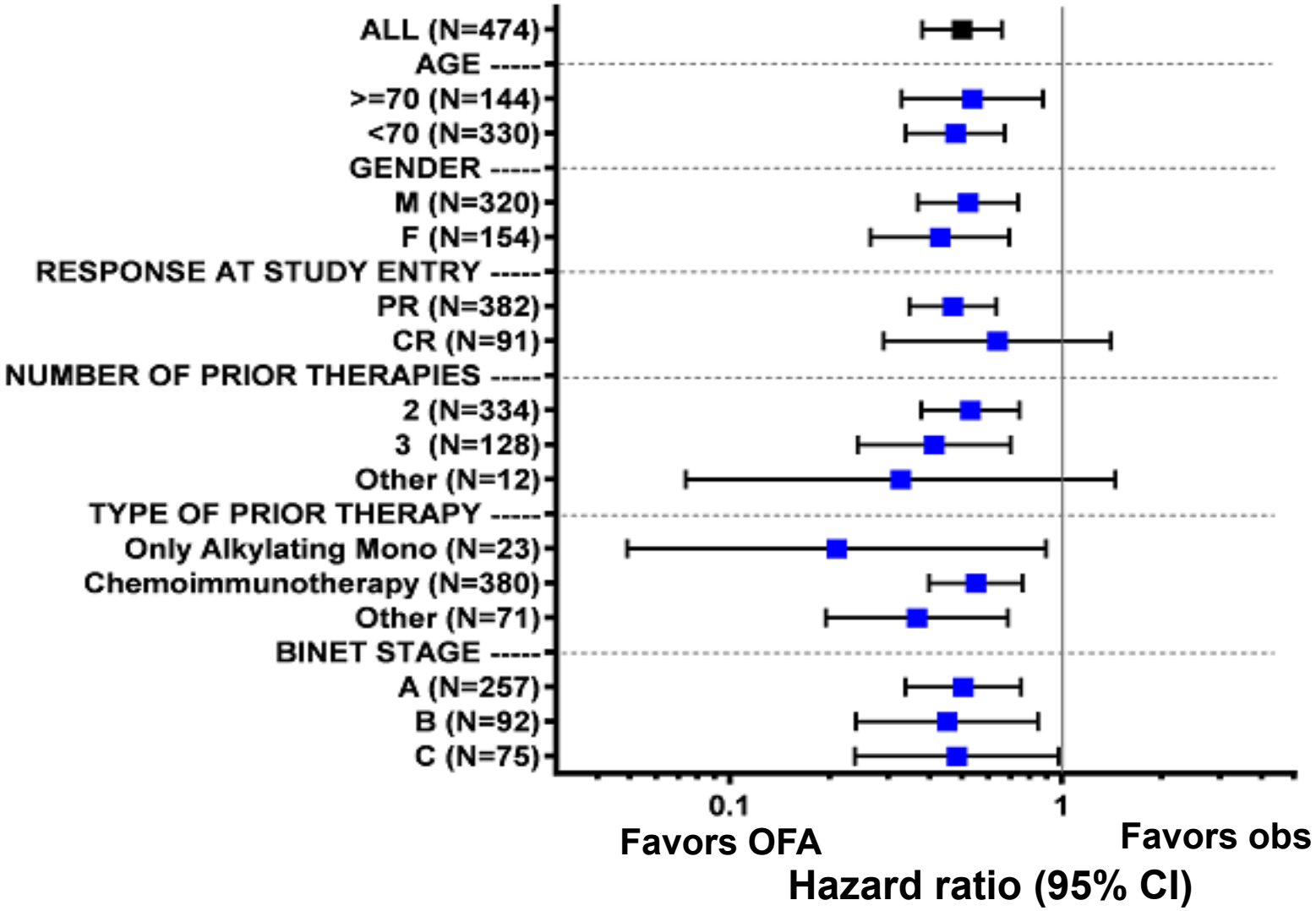
Median follow-up: 19.1 months



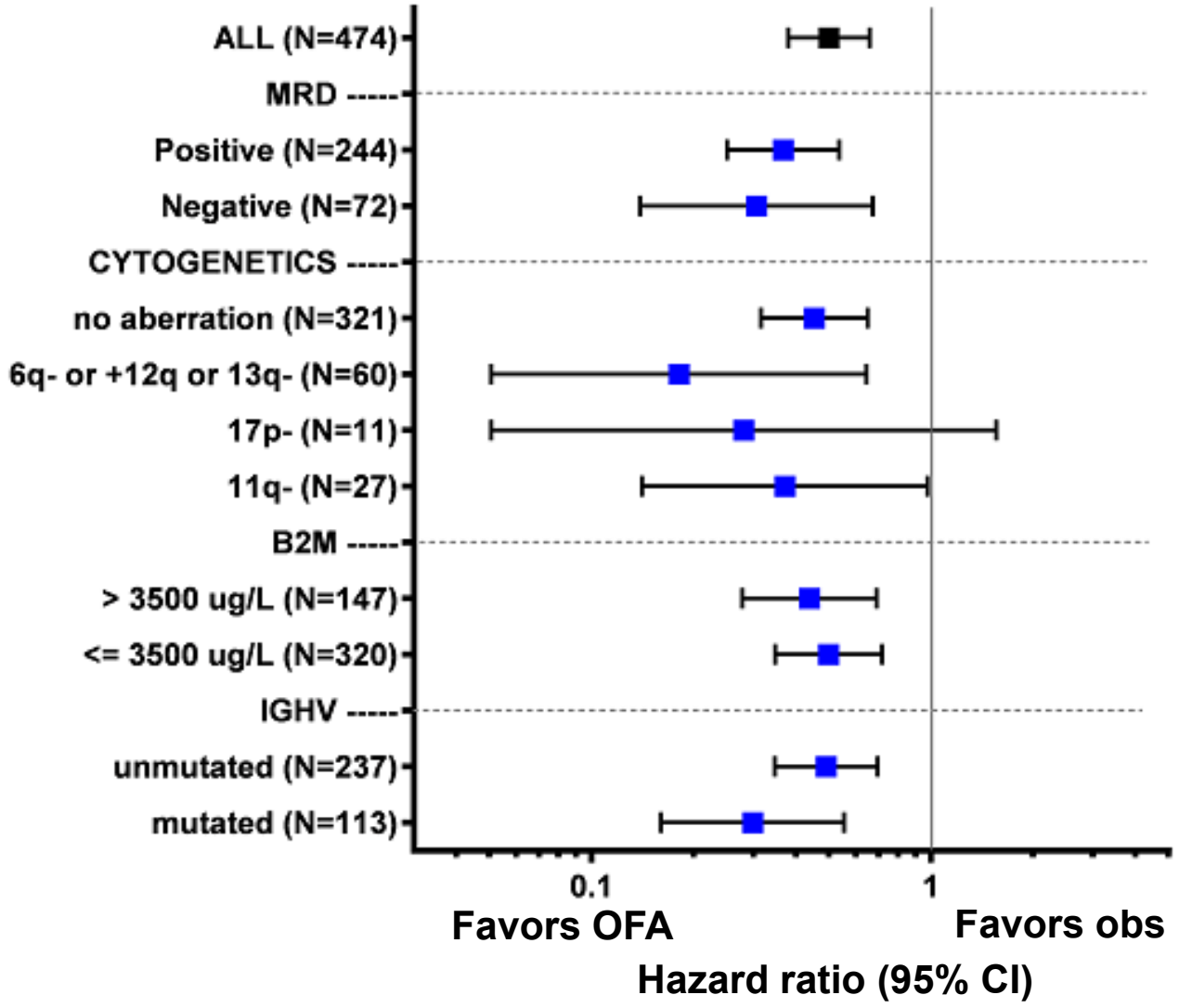
Number of Subjects at Risk:							
Ofatumumab	238	191	145	110	81	49	25
Observation	236	161	106	69	46	26	13

stratified log-rank test

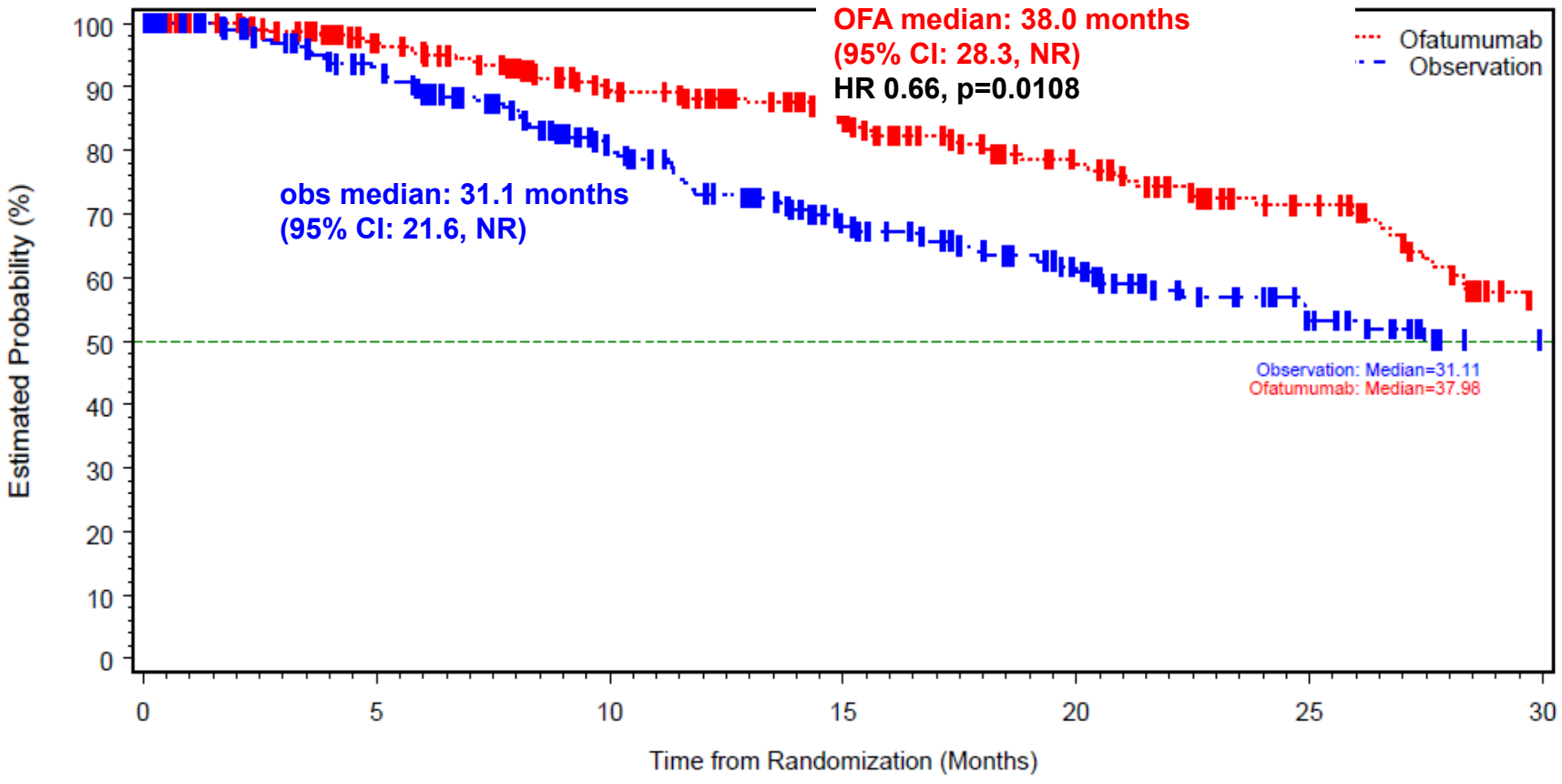
PROLONG: PFS Subgroup Analysis



PROLONG: PFS in Prognostic Subgroups

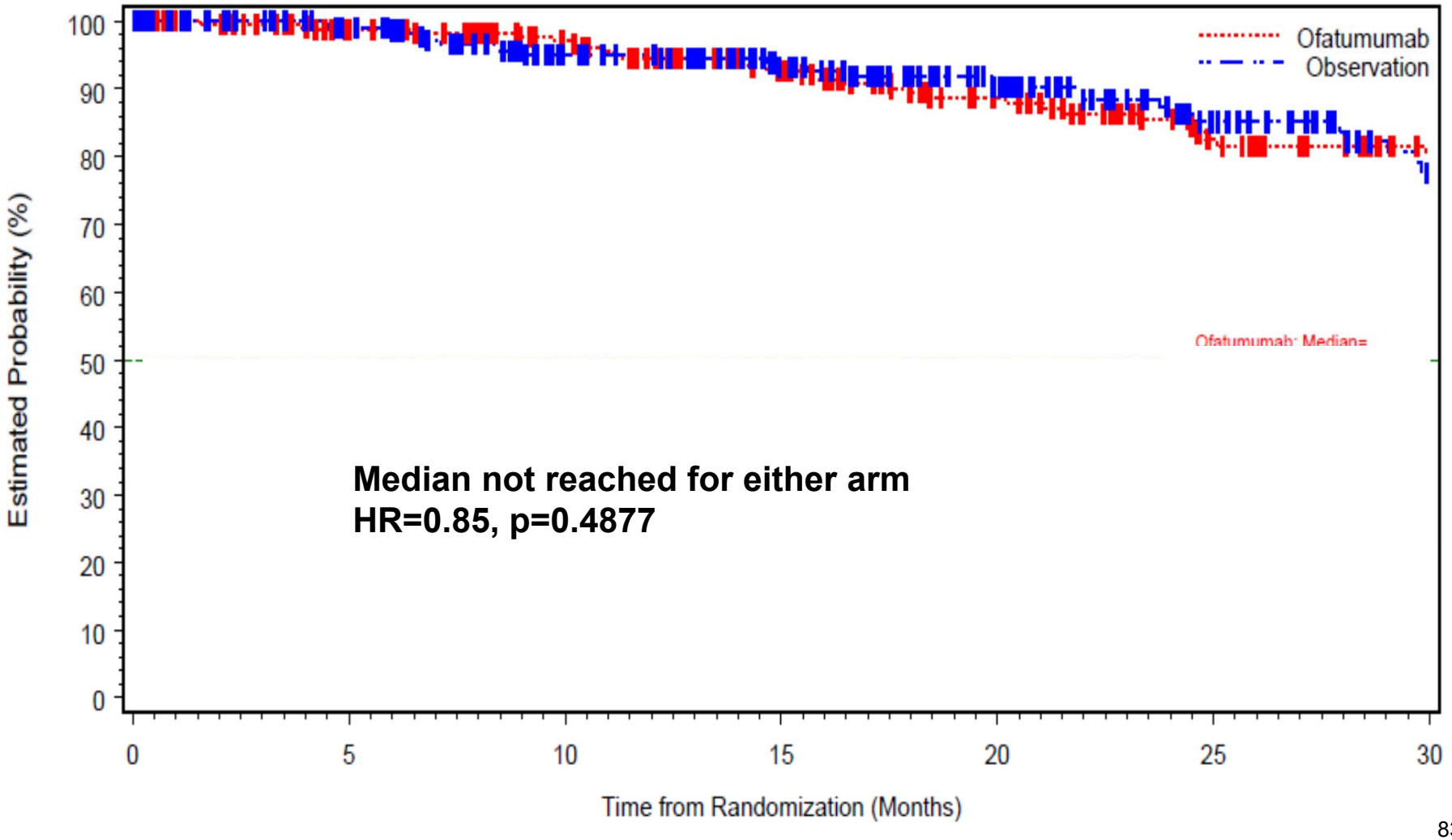


PROLONG study: Time to next treatment



stratified log-rank test

PROLONG study: Overall Survival



Median not reached for either arm
HR=0.85, p=0.4877

stratified log-rank test

PROLONG study: Conclusions from interim analysis

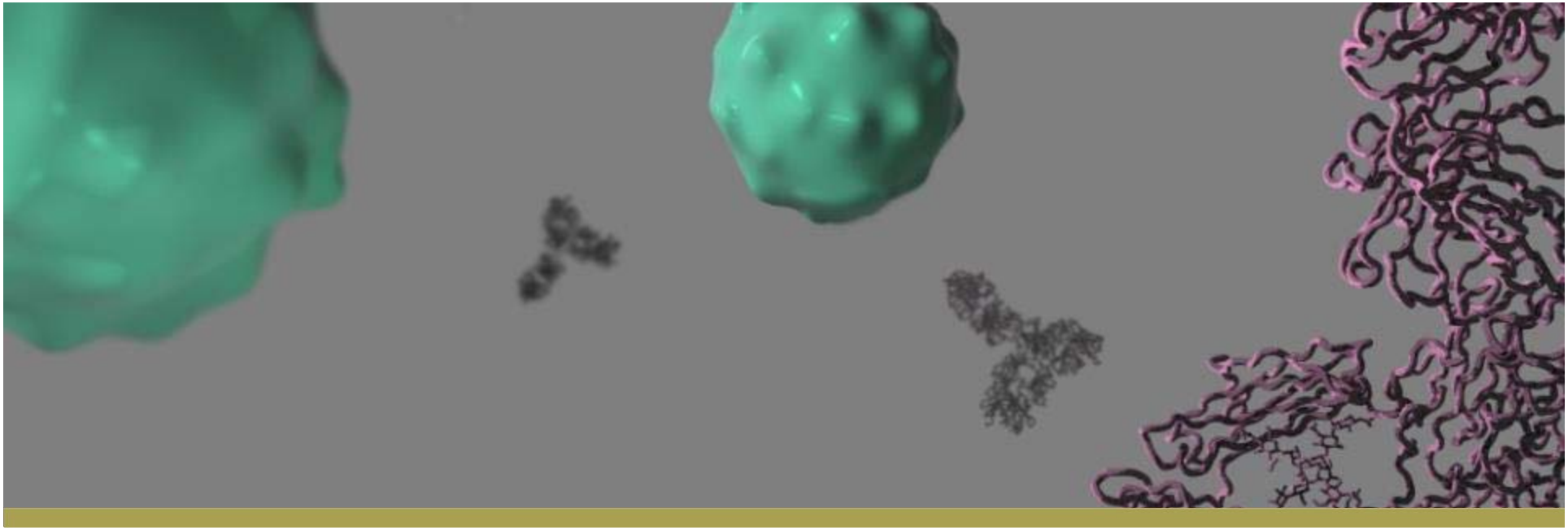
Ofatumumab maintenance treatment in relapsed CLL:

- Results in a highly significant and clinically meaningful improvement of PFS
- Significantly prolongs time to next treatment
- Is well tolerated
- Is associated with an AE profile characteristic of anti-CD20 therapy i.e. increased incidence of neutropenia and infections

Acknowledgments

We would like to thank all the patients who participated in the study and the investigators from all study sites (listed alphabetical last name) and their site staff for their contributions

Drs. Abdulkadyrov, Afanasyev, Aktan, Anagnostopoulos, Aurran, Aviv, Bairey, Braester, Ben-Yehuda, Borbenyi, Carney, Carter, Casado Montero, Cazin, Chagorova, Chen, Cherif, Chiattone,Cho,Daenen, de Araujo, de Castro, de la Cruz Vincente, Del Poeta, Deenik, Deeren, Dilhuydy, Domnikova, Drenou, Enrico, El Yamani, Enggaard, Feugier, Fineman, Fijnheer, Gaidano,Gollard,Gonzalez Barca,Gonzalez Diaz, Grasa-Ulrich, Grosicki, Herishanu, Homenda, Iles, Ilhan, Irwin, Jamshed, Jedrzejczak, Jung, Kampen, Kaplan, Kaplanov, Kendall, Kioumi, Kimby, Kloczko, Klueppelberg, Kryachok, Kuliczkowski, Kulyaba, Kuzmin, Lange, Laptalo, Lauri, Leeksma, Leijs, Lepine-Martin, Levin, Lindstrom, Lotfi, Lugtenburg, Lysa, Ma, MacEachern, Marjit, Marasca, Masszi, Mayer, Mavromatis, Melikyan, Mulvey, Nagler, Nagovski, Offner, Olney, Oliynyk, Opat, Osmanov, Owen, Pajkos, Panagiotidis, Papajik, Park, Pavlovksy, Pectasides, Peles, Perez Saenz, Petrini, Poulsen, Prujit, Pylypenko, Rahimi-Levene, Ramanan, Repousis, Ruchlemer, Sankelo, Sayinalp, Schipperus, Schwartzberg,Sender, Sengar, Shah, Smolej, Somer, Spaner, Stewart, Tadmor-Meyuchas, Tavares, Theunissen, Tjonnsford, Tombuloglu, Tournilhac, Trullemans, Vallisa, van Hoof, Vilque, Viola, Vitolo, Wallentine, Yuklea, Zachee, Zunic



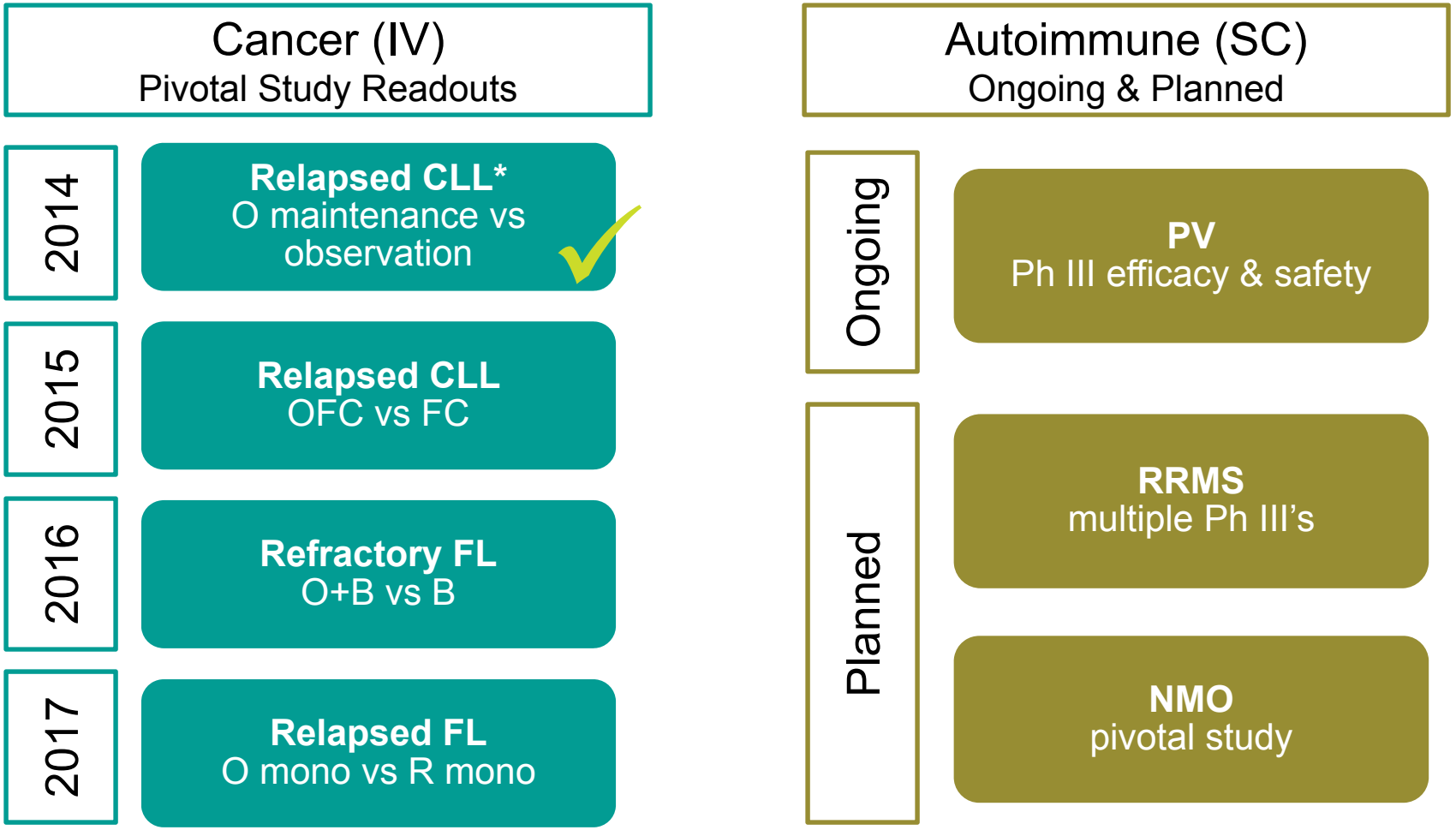
Ofatumumab

Presented by Jan van de Winkel

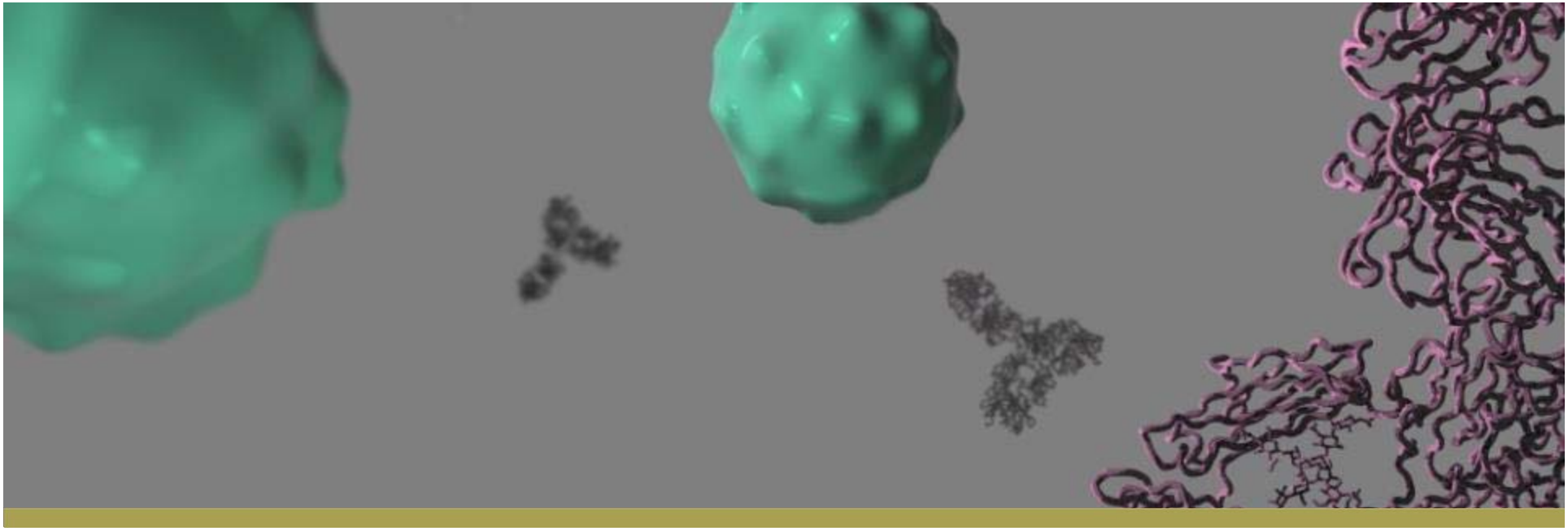
CEO, Genmab

Genmab

Ofatumumab: Planned & Ongoing Trials



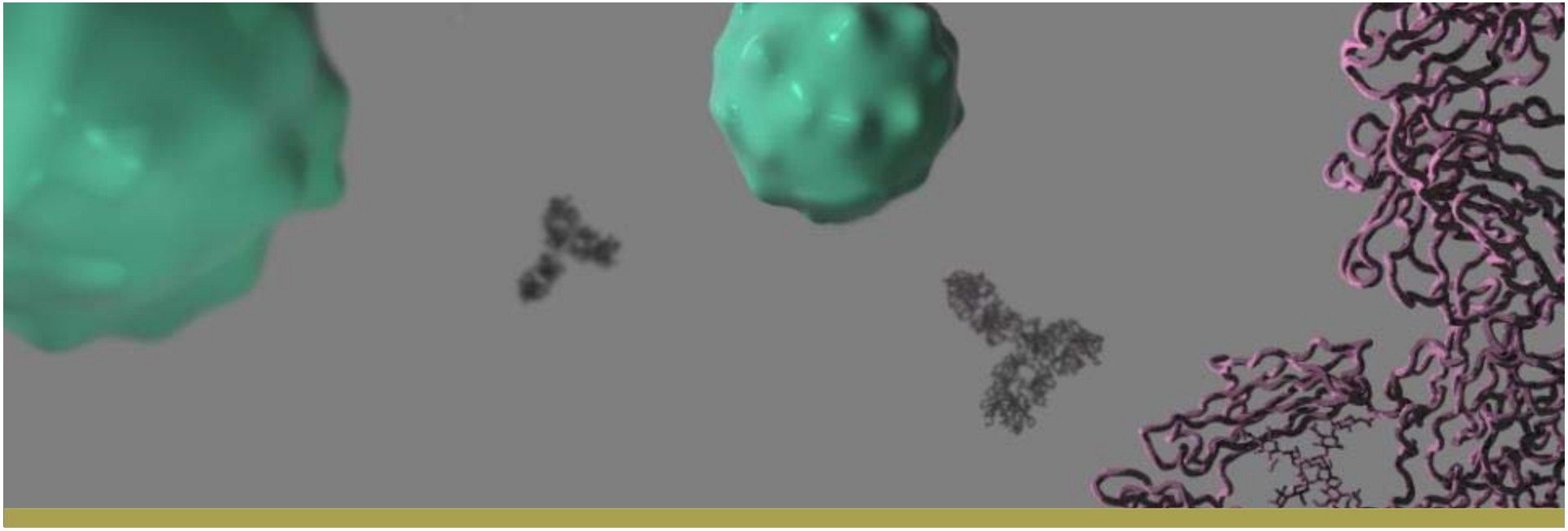
Note: The indications above are unapproved
*Interim data reported



Ofatumumab Q&A

Prof. Marinus Van Oers, *Academic Medical Center Amsterdam;*
Steen Lisby & Jan van de Winkel, *Genmab*

Genmab



HuMax-TF-ADC

Presented by Steen Lisby, MD, DMSc

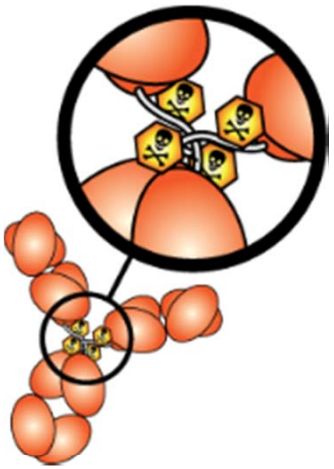
Senior Medical Director, Genmab

Genmab

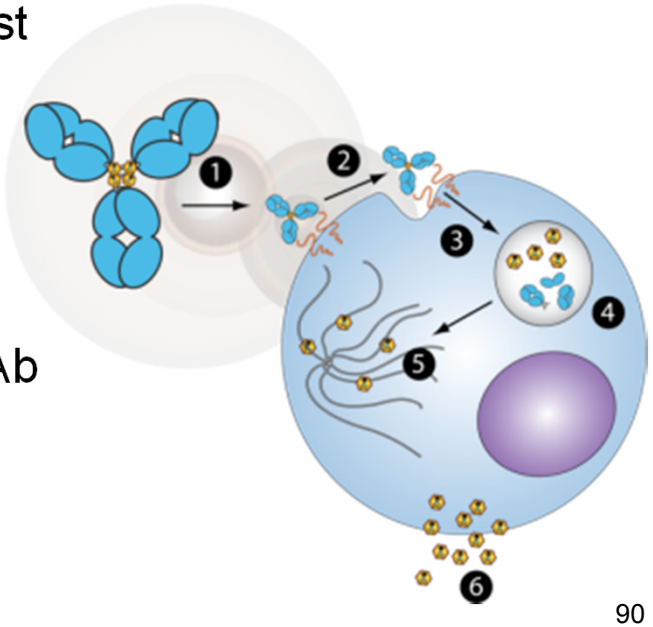
HuMax-TF-ADC

HuMax-TF-ADC is an antibody drug conjugate composed of:

- A human monoclonal antibody specific for tissue factor
- A protease-cleavable valine-citruline linker
- The tubulin inhibitor monomethyl auristatin E (MMAE); a synthetic dolastatin analogue



After binding, internalization and degradation, MMAE binds tubulin thus driving the cell to cell cycle arrest followed by apoptotic cell death



Tissue Factor (TF; CD142):

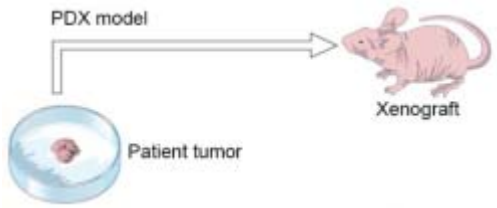
- Overexpressed on many solid tumors

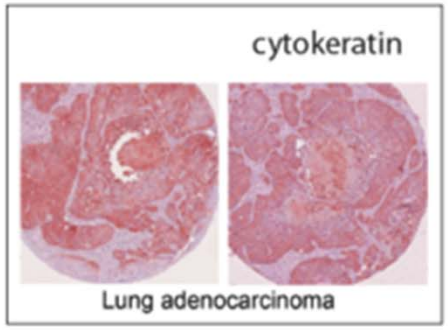
HuMax-TF-ADC combines the specificity of TF mAb with the cytotoxicity of MMAE

Doronina et al. Nat. Biotechnol. 21:778—784 (2003)
Breij et al. Cancer Res. 74: 1214 – 26 (2014)

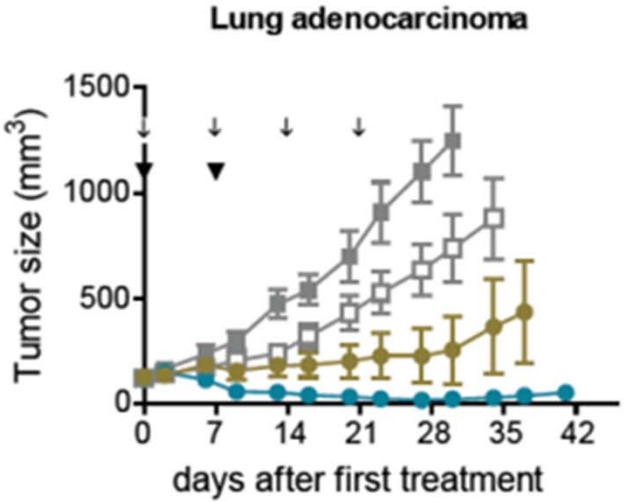
HuMax-TF-ADC Induces Tumor Regression

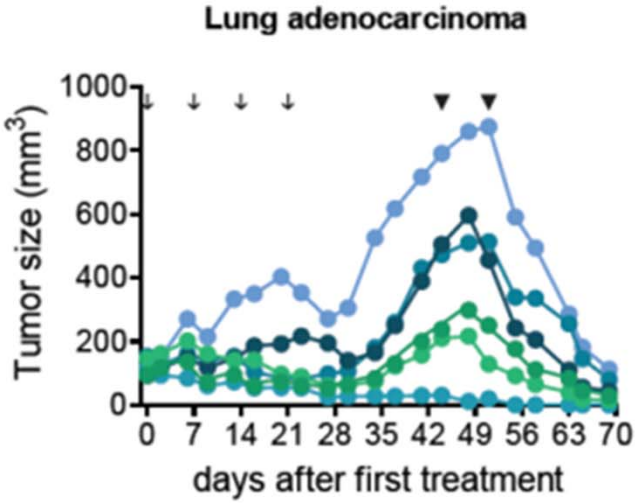
High TF Expressing - Lung Adenocarcinoma PDX Model





>75% TF⁺ cells





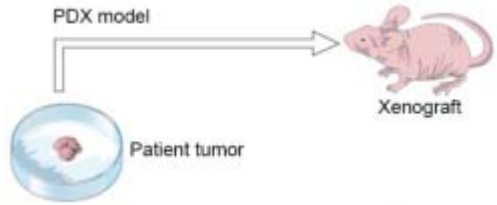
- TF-011-MMAE
- b12-MMAE (isotype ctrl ADC)
- b12 (isotype ctrl IgG1)
- paclitaxel

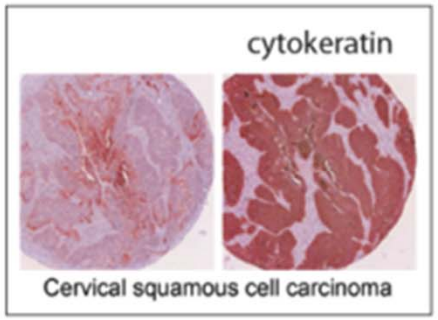
↓ Treatment paclitaxel

▼ Treatment ADC

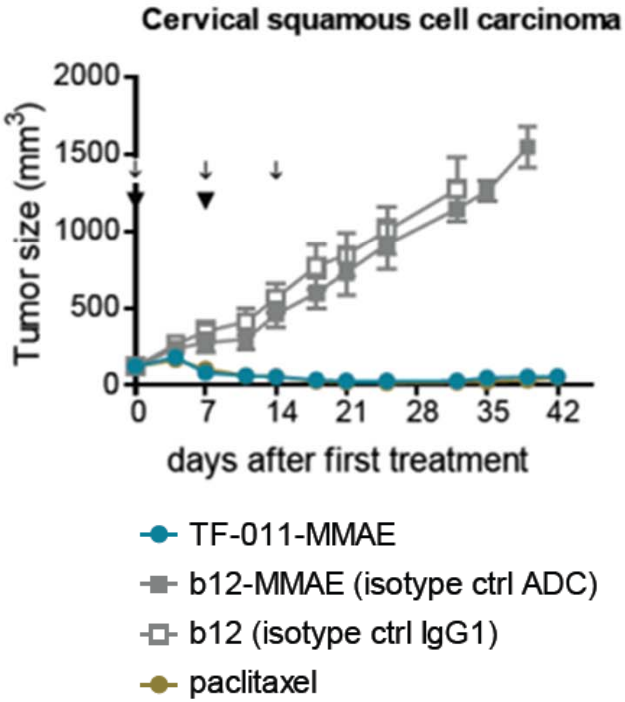
HuMax-TF-ADC Induces Tumor Regression

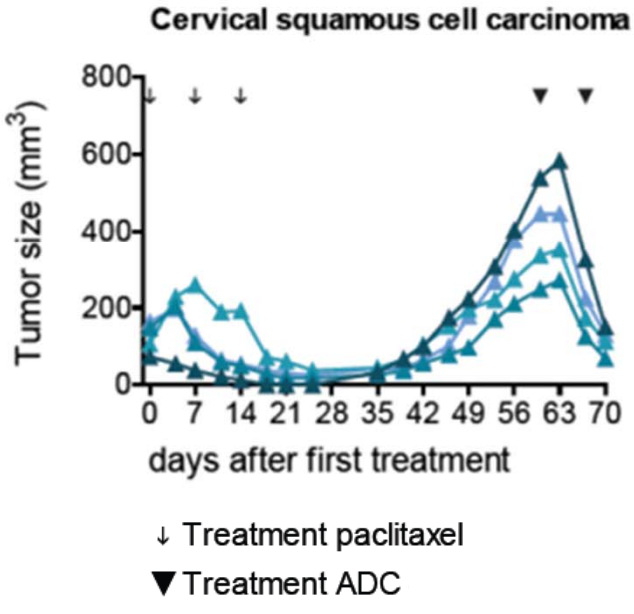
Low TF Expressing – Cervical Squamous Cell PDX Model





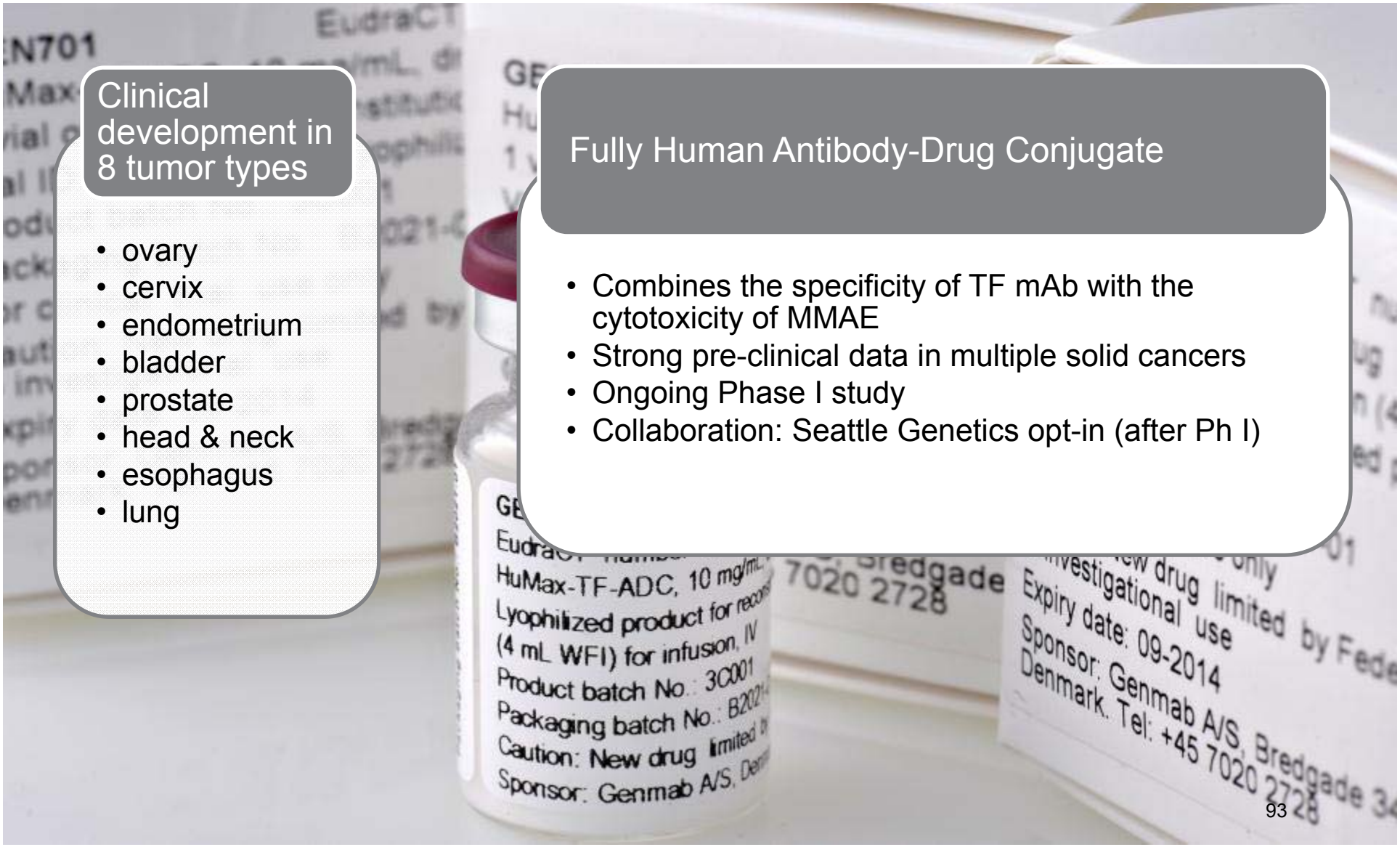
25-50% TF⁺ cells





HuMax-TF-ADC: In the Clinic

Next Generation Therapeutics



Clinical development in 8 tumor types

- ovary
- cervix
- endometrium
- bladder
- prostate
- head & neck
- esophagus
- lung

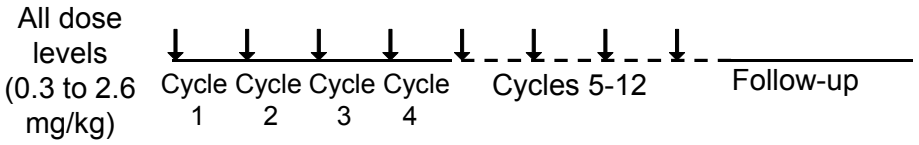
Fully Human Antibody-Drug Conjugate

- Combines the specificity of TF mAb with the cytotoxicity of MMAE
- Strong pre-clinical data in multiple solid cancers
- Ongoing Phase I study
- Collaboration: Seattle Genetics opt-in (after Ph I)

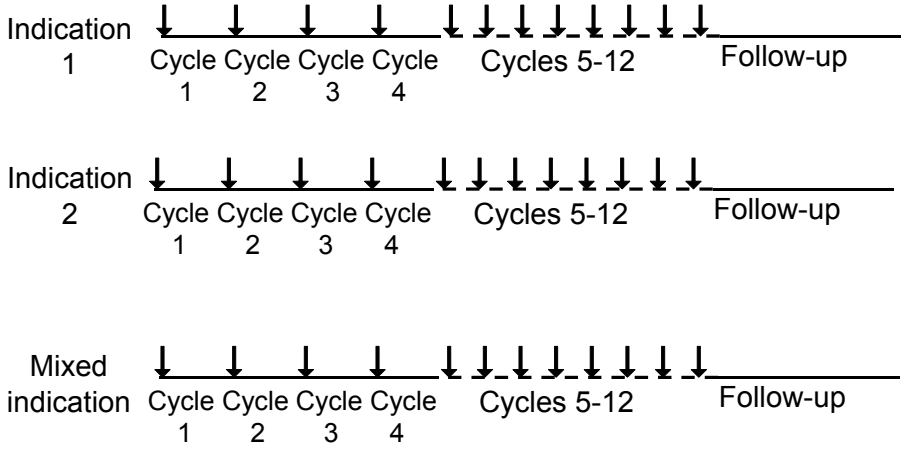
HuMax-TF-ADC: Phase I Study

- Phase I, 54 patients; primary endpoints: safety and tolerability
  - Recruits at MD Anderson, Texas; Royal Marsden, London and Copenhagen University Hospital, Copenhagen
  - Part 1, dose escalation in pts. with advanced and / or metastatic solid tumors who have failed or are not candidates for standard therapy
  - Part 2, cohort expansion will further explore recommended Ph II dose of HuMax-TF-ADC as determined in Part 1

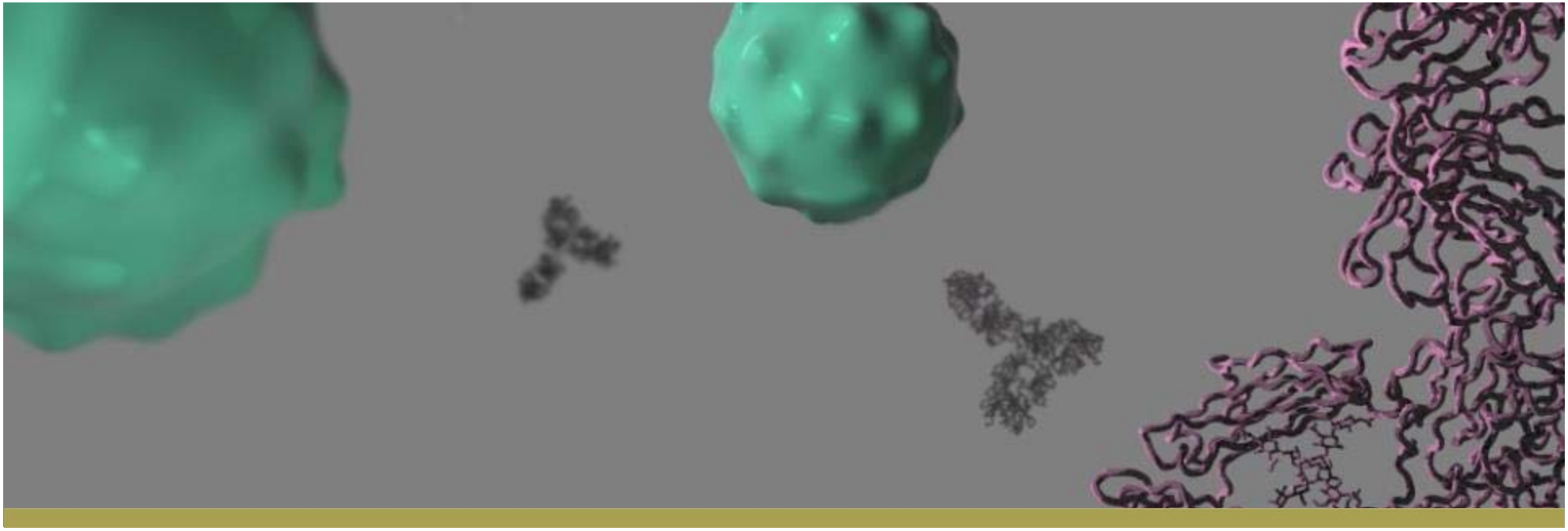
Part 1: 3 (+3) pts. per cohort



Part 2: 10 pts. per cohort at recommended Phase II dose



↓ HuMax-TF-ADC infusion on day 1 of cycle
Each treatment cycle is 3 weeks
- - - - - - Optional



Pre-Clinical Pipeline – The Antibody Experts

Building a Robust Innovative Pre-Clinical Pipeline

Presented by Jan van de Winkel

CEO, Genmab

Genmab

Building a Robust Innovative Pipeline

>20 pre-clinical projects ongoing

- DuoBody & HexaBody platform products & ADC products
- Pipeline delivers multiple chances for success & includes Genmab owned and partner products

HuMax-AXL-ADC announced

- ADC technology from Seattle Genetics
- Potential for Seattle Genetics to increase royalties prior to Phase III

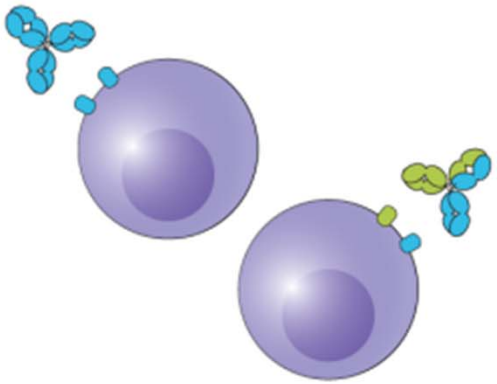
Creating value from proprietary technologies

- Progressing DuoBody platform commercial partnerships with Janssen & Novartis
- First HexaBody platform research collaborations announced

Genmab Product Focus

Oncogenic Drivers

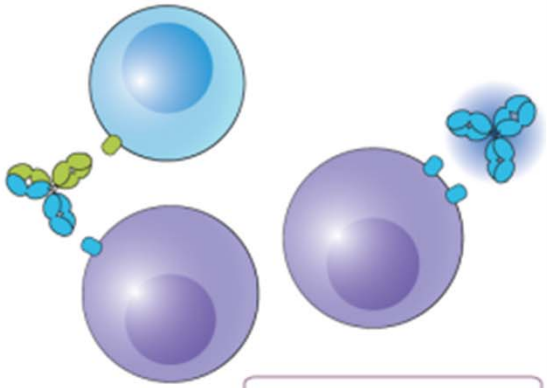
Targeting tumorigenic signaling pathways



DuoBody-AxB

Engagement Immune System

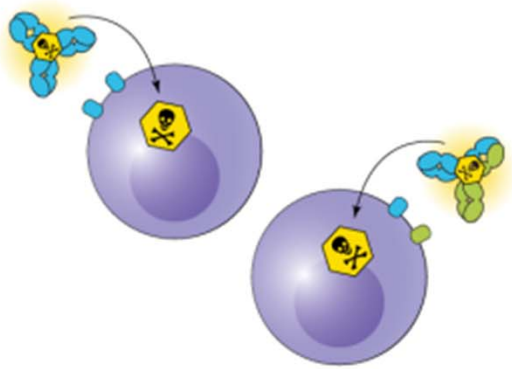
Immunomodulation
Recruitment effector cells, T cells
Recruitment effector components, CDC/ADCC



ofatumumab
daratumumab
HexaBody-X
DuoBody-CD3xA/B/...

Antibody-Drug Conjugates

Toxin-mediated cell kill



HuMax-TF-ADC
HuMax-AXL-ADC
HuMax-TAC-ADC
DuoBody-AxB-ADC

Genmab's Innovative Pre-Clinical Pipeline

DuoBody™ formats

- DuoBody-CD3 bispecific shows dose dependent lysis of hematological cancer cells by T cells
- Prototypic DuoBody-ADC product candidate shows efficient killing of hematological cancer cells

HexaBody™ format

- HexaBody molecules directed towards a hematological cancer target kill primary cancer cells via CDC much more effectively than a reference IgG1 antibody

Immuno-Oncology

Turning Cancer into a Chronic Condition

Hottest Area in Oncology

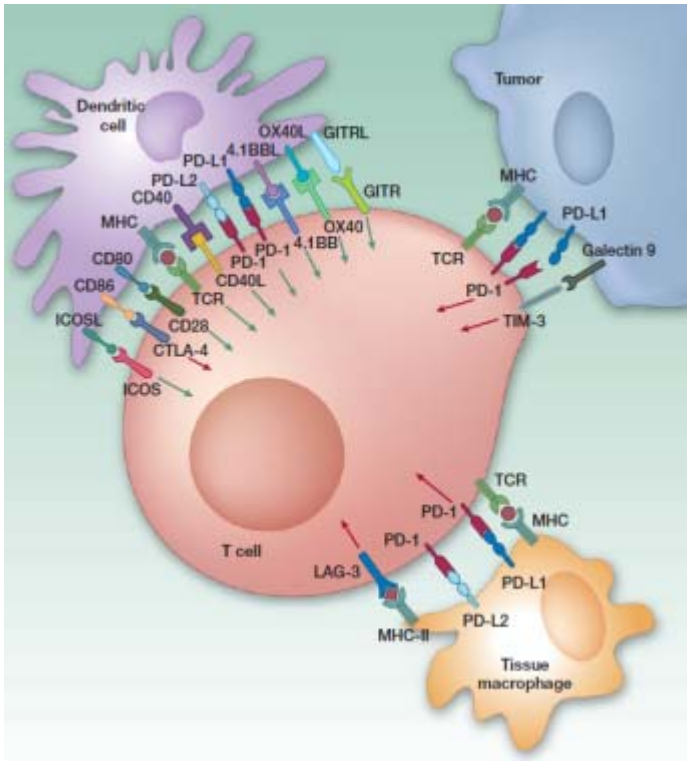
- Long duration of response
- Potential game changer
  - $35B market

Many Immune Check Point Targets

- Combinations may improve survival outcome

DuoBody

- Robust & versatile BsAb platform
- Ideal for:
  - Screening multiple combinations in final therapeutic format
  - Combined targeting immune check points

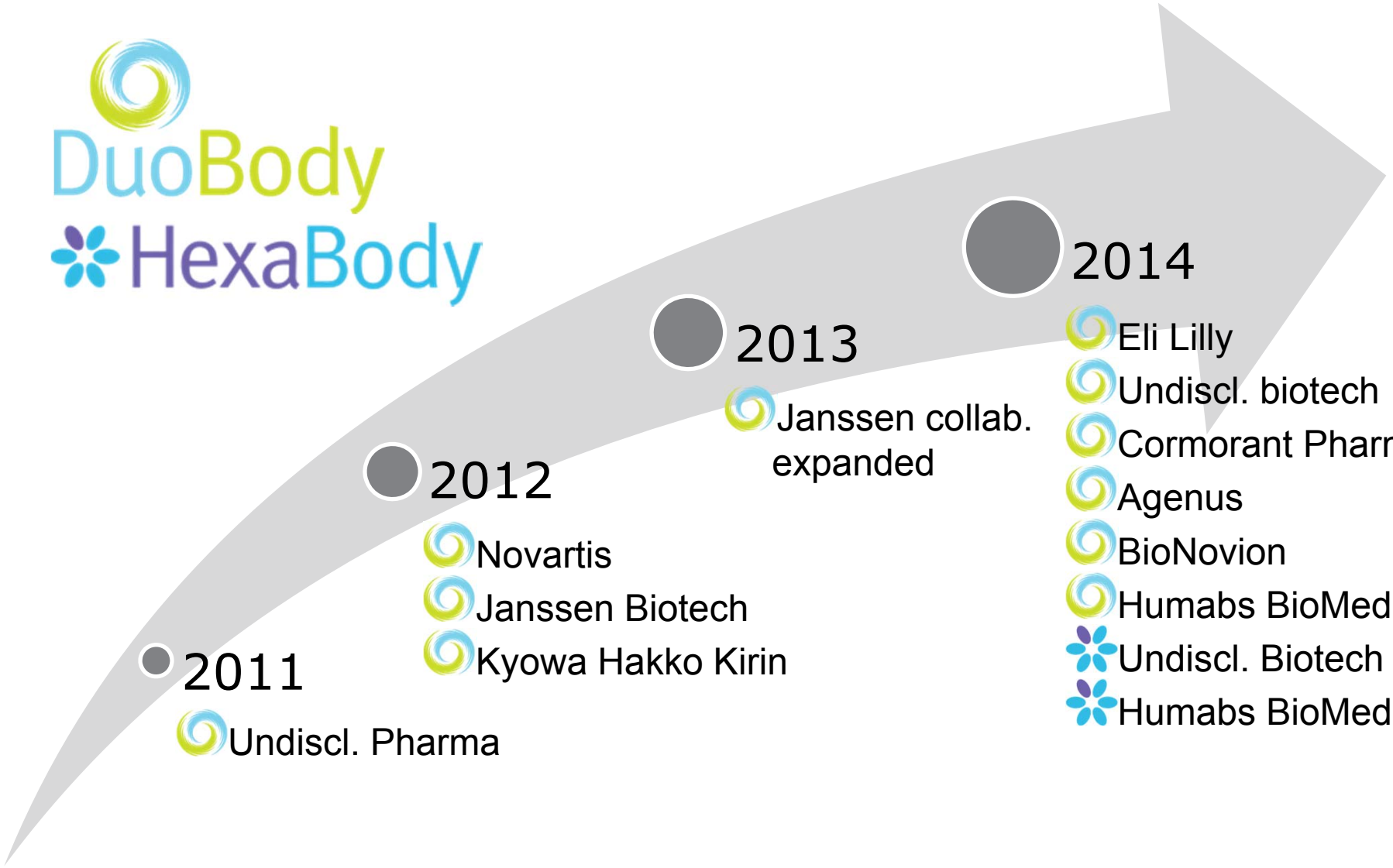


Ott et al. Clin Cancer Res. 2013

Progressing DuoBody & HexaBody Partnering

DuoBody

HexaBody



HuMax-TAC-ADC

Combining HuMax-TAC with a PBD-Based Warhead

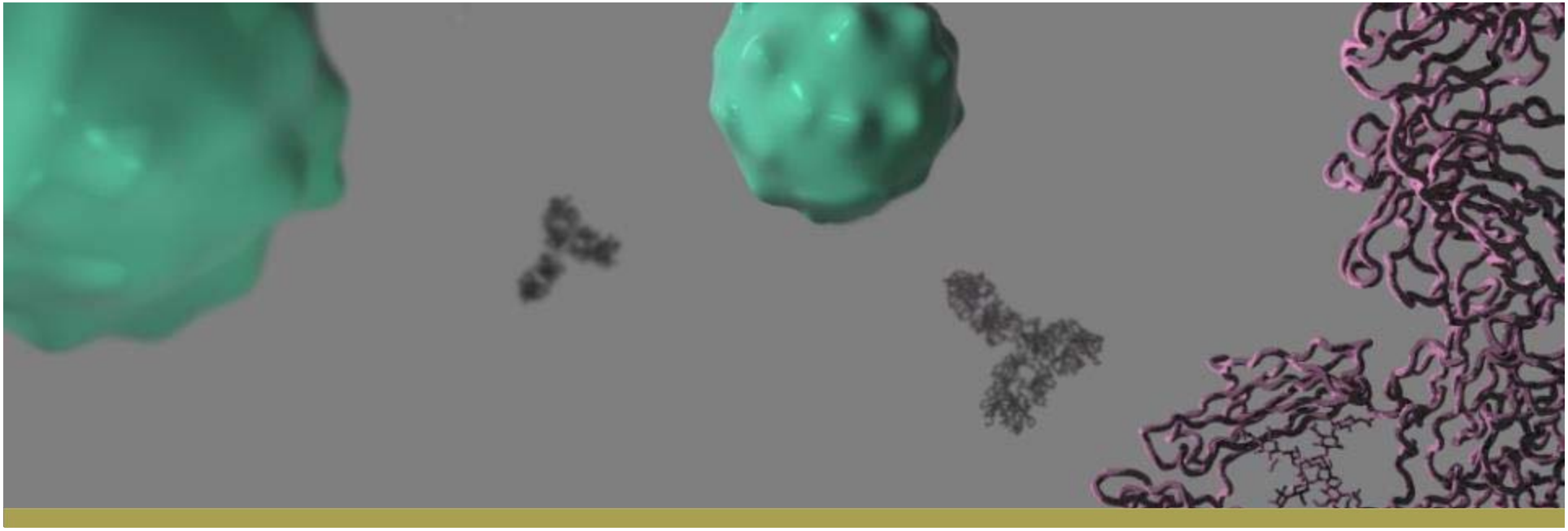
- Targets TAC (CD25, IL2Rα) expressed on many hematological cancers
- HuMax-TAC-ADC (ADCT-301) shows robust dose-dependent anti-tumor activity in xenografts
- Collaboration: ADC Therapeutics

M.J. Flynn et al. ASH 2014, abstract #71609

HuMax-AXL-ADC Efficacy in *in vivo* Tumor Model

Fully Human Antibody-Drug Conjugate

- Targets AXL signaling molecule expressed on many solid cancers
- HuMax-AXL-ADC shows anti-tumor activity in patient-derived xenograft model with heterogeneous target expression
- Collaboration: Seattle Genetics



Innovative Approaches to Recruit Complement by Novel Antibody Therapeutics

Presented by Prof. Thomas Valerius
University Hospital Schleswig-Holstein

Genmab

Innovative approaches to recruit complement by novel antibody therapeutics

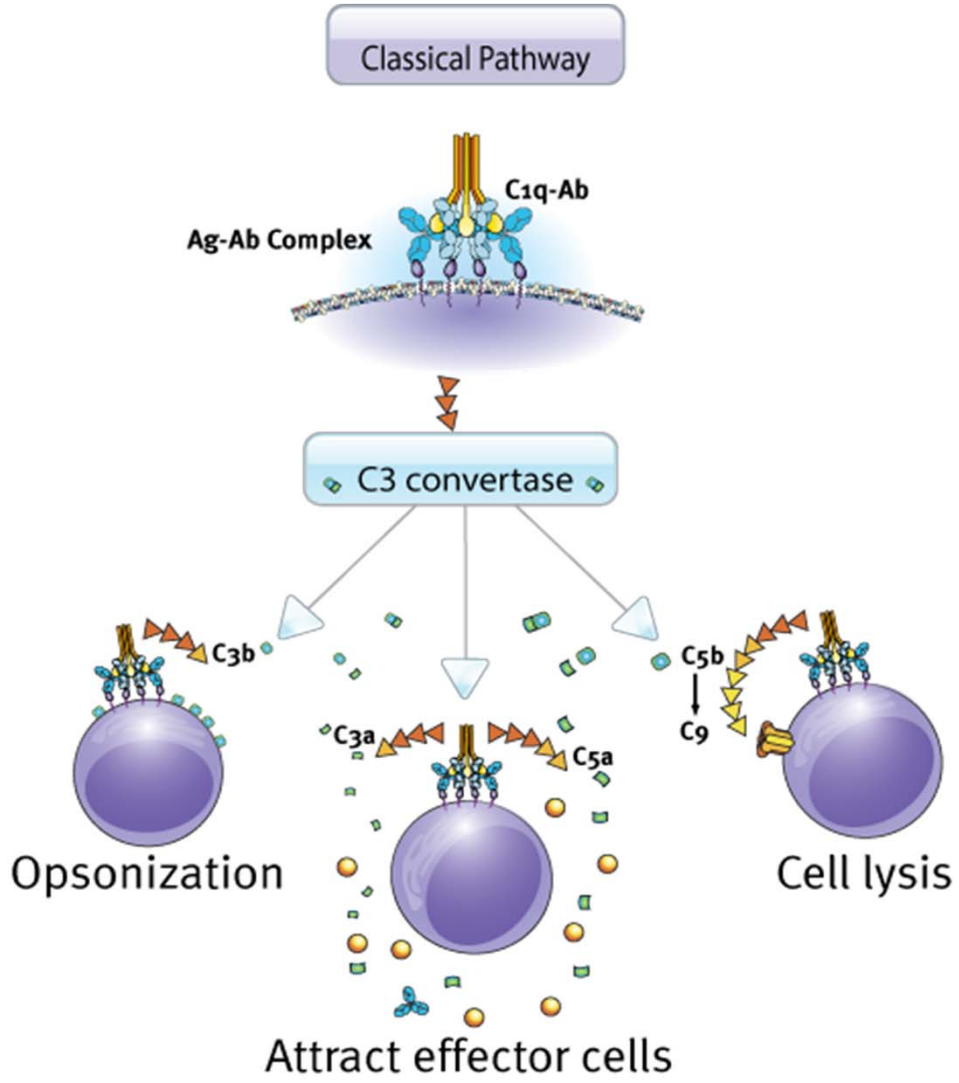
Thomas Valerius, MD

Division of Stem Cell Transplantation and Immunotherapy

Christian-Albrechts University, Kiel, Germany

UK
SH

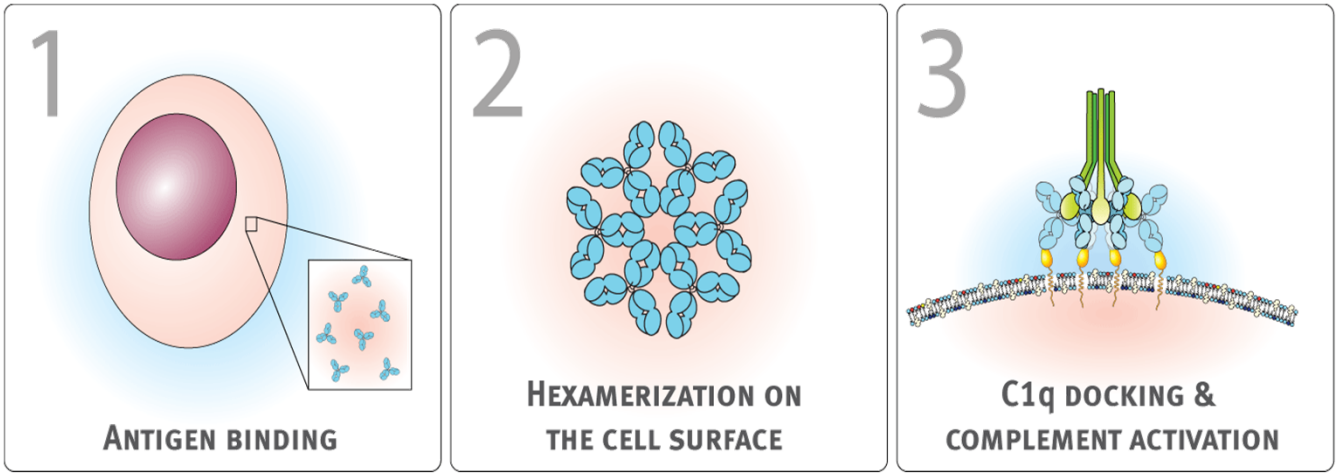
Complement as potent effector mechanism



Involved in the mode of action for antibodies against CD20, CD38, CD52 and others

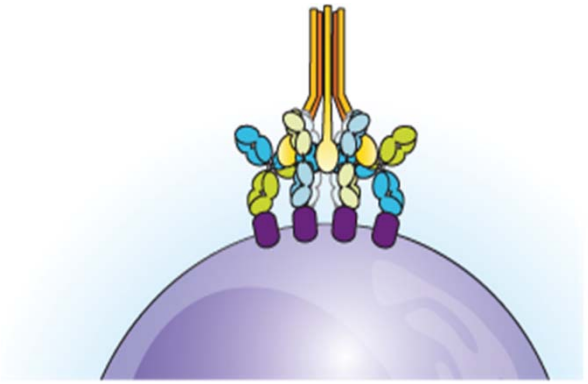
Hexamerization on the cell surface: Effective C1q binding and CDC

1. Antibody molecules bind to target antigens on the cell surface
2. Hexamerization occurs through Fc:Fc interactions
3. Hexamerization is critical for optimal C1 binding, complement activation and complement-mediated killing



Diebolder et al. Science 343:1260, 2014

Fc:Fc interactions can be manipulated to enhance complement activation



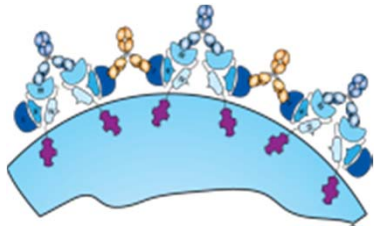
HexaBody™ technology

enhanced Fc:Fc interactions

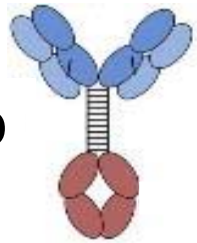
The HexaBody technology induces CDC activity of EGFR and type II CD20 antibodies

Approaches to enhance CDC

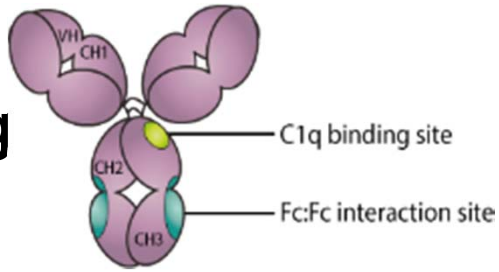
- non-cross-blocking antibody combinations



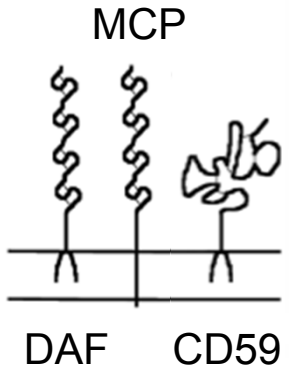
- switching to the IgG3 isotyp



- Fc engineering



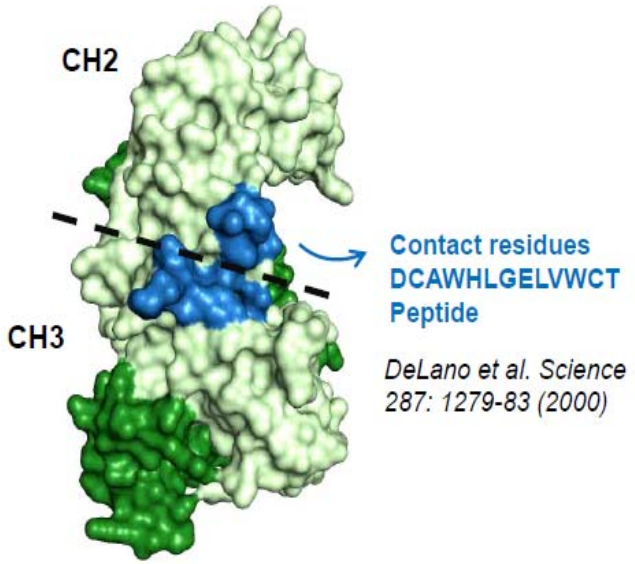
- inhibiting complement regulatory proteins (CRP)



HexaBody technology in comparison to competitors

The HexaBody technology outperforms the tested technologies which employ enhanced C1q-binding

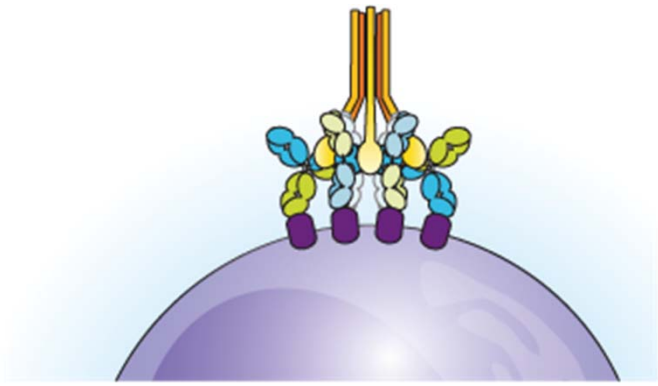
HexaBody molecules trigger CDC by a distinct mode of action



DeLano peptide
binds residues in the Fc-Fc interface

HexaBody molecules trigger CDC by a distinct mode of action

Conclusions



HexaBody technology…

… enhances Fc:Fc interactions upon target antigen binding

… enhances CDC activity through a distinct mode of action

... outperforms the tested technologies which employ enhanced C1q-binding

... can be employed for a range of therapeutic target antigens (e.g. CD20, EGFR) and a variety of clinical indications

Co-workers

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Yasmin Brodtmann

Kathinka Tüxen

Annalina Tammen

Thies Rösner

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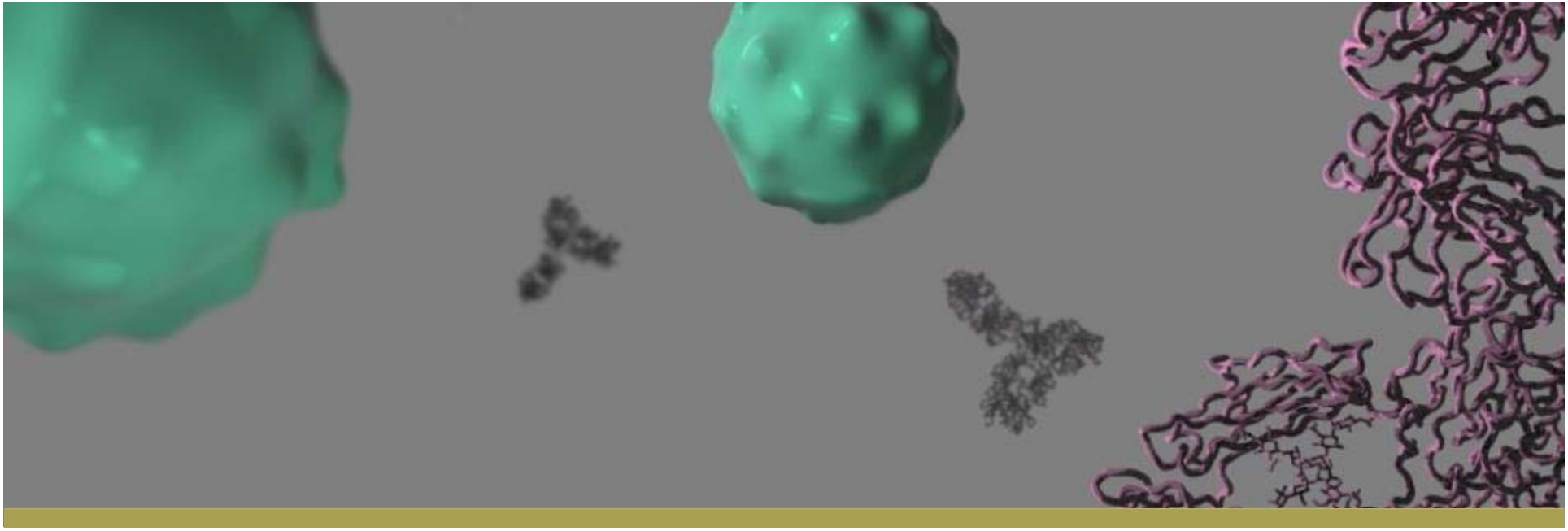
Rob de Jong

Janine Schuurman

Paul Parren

supported by funding from the DFG, WSF, CAU and Genmab



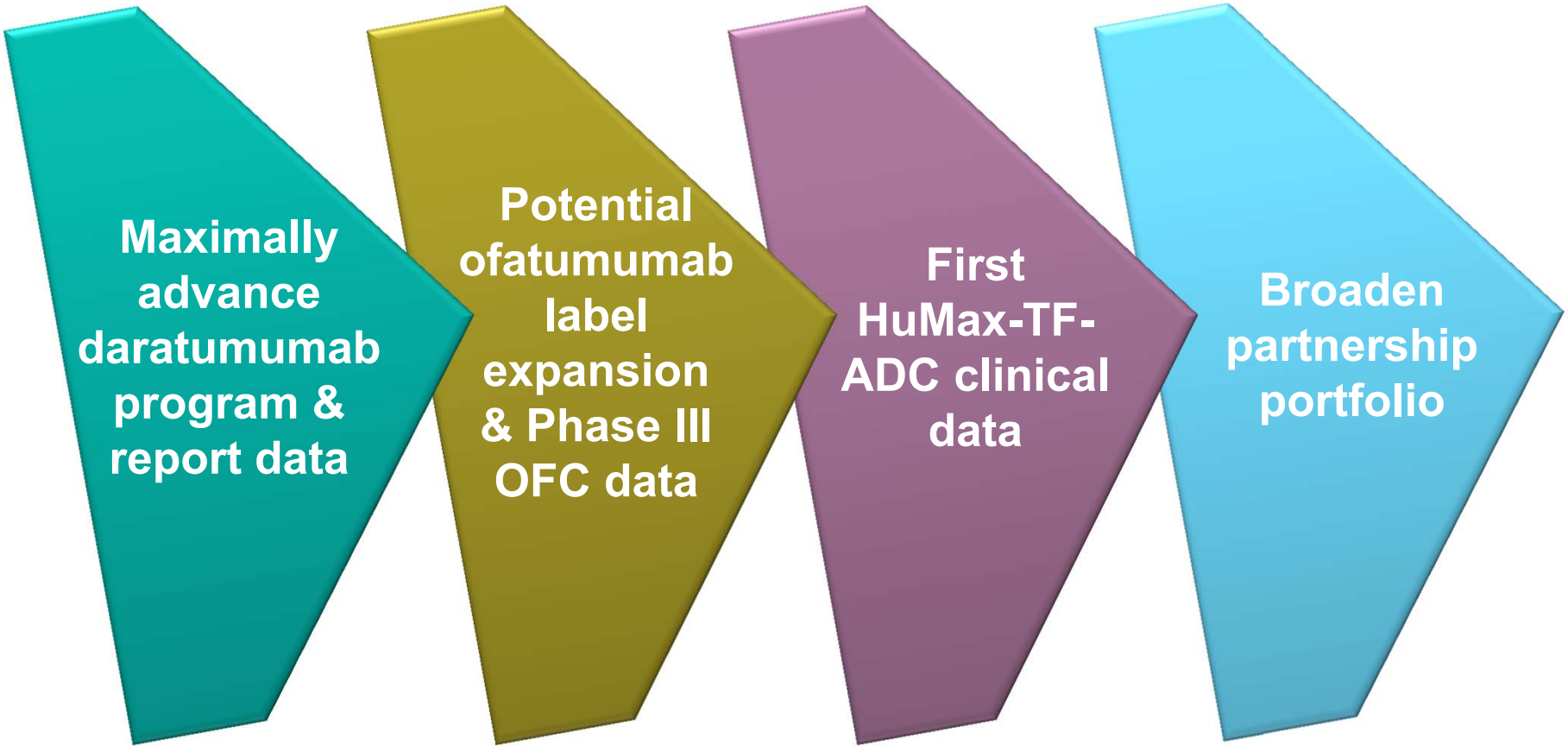
The Year Ahead

Presented by Jan van de Winkel

CEO, Genmab

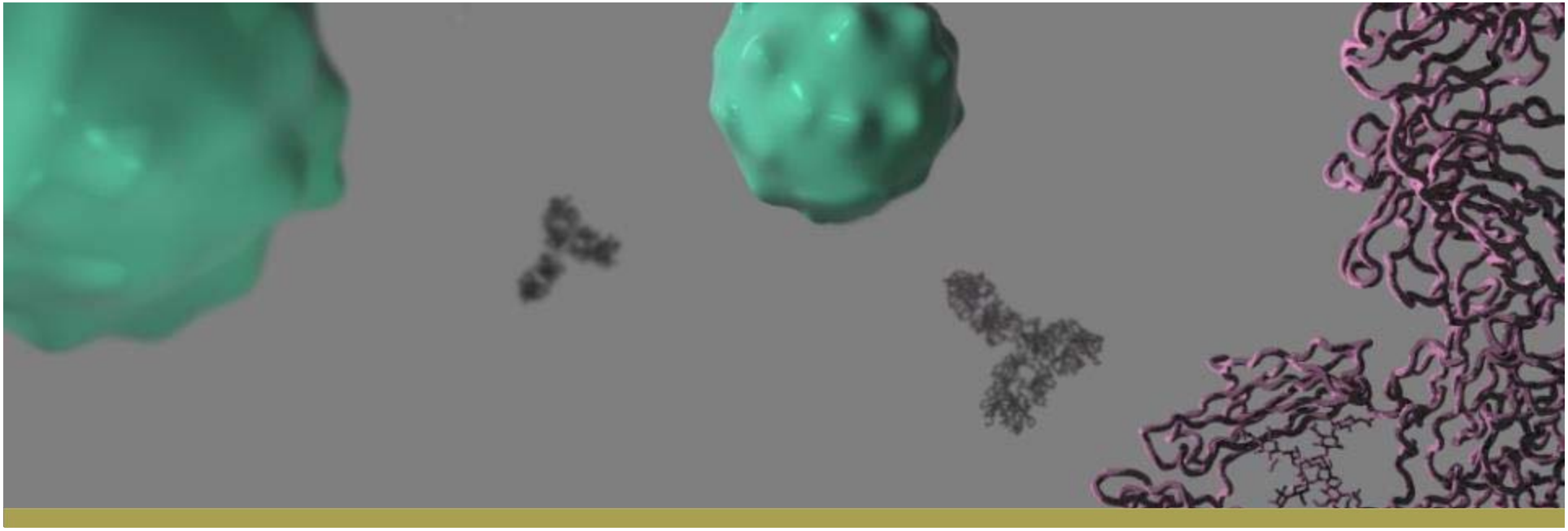
Genmab

An Exciting Year Ahead



2015 Goals: Maximizing Pipeline Value

Priority	Targeted Milestone
Maximize daratumumab clinical progress	» Phase II MM monotherapy data & - if favorable, discuss regulatory next steps with health authorities » Start multiple new MM trials » Start non-MM clinical trial
Optimize ofatumumab value	» File for an additional indication » Phase III relapsed CLL data » Start Phase III sc autoimmune trials
Strengthen differentiated product pipeline	» Phase I HuMax-TF-ADC data » Progress HuMax-AXL-ADC » Progress pre-clinical DuoBody & HexaBody projects
Broaden partnership portfolio with next generation technologies	» Expand DuoBody & HexaBody collaborations » Progress partnered programs » New IND filings
Disciplined financial management	» Maintain cost base while selectively investing to advance pipeline



Q&A

Jan van de Winkel & David Eatwell, *Genmab*

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Glædelig Jul og Godt Nytår

Holiday Greetings

Prettige Feestdagen

Copenhagen • Princeton • Utrecht