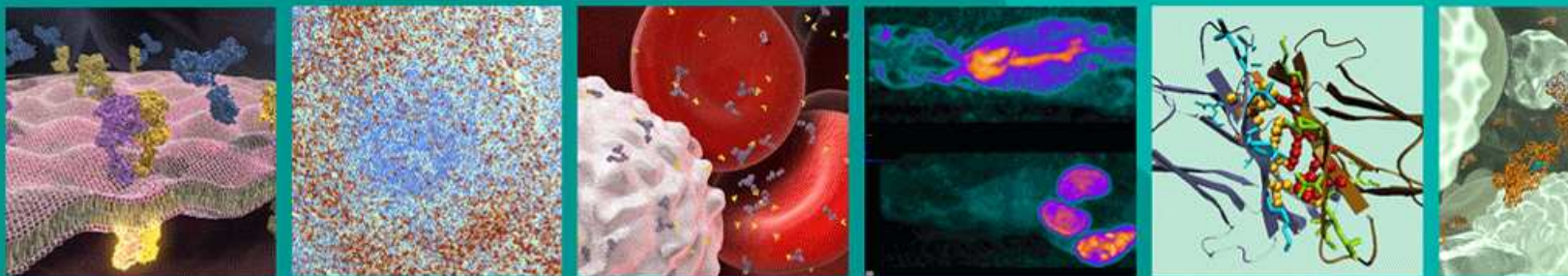




Genmab Post ASH Seminar 19 December 2011

Presenter: Jan van de Winkel, Ph.D.
President and CEO Genmab A/S



Agenda

2:30 PM	Arrival	
2:45 PM	Introduction and agenda	<i>Jan van de Winkel, Genmab</i>
3:10 PM	Ofatumumab in relapsed or refractory aggressive B-cell lymphoma Q&A	<i>Prof. Anton Hagenbeek Academic Medical Center Amsterdam</i>
3:45 PM	A phase II trial of ofatumumab in subjects with Waldenström's macroglobulinemia Q&A	<i>Steen Lisby, Genmab</i>
4:00 PM	A phase I/II, dose-escalation study of daratumumab, a CD38 mAb in patients with multiple myeloma Q&A	<i>Prof. Torben Plesner Vejle Hospital, Arhus</i>
4:30 PM	Next steps / Q&A	<i>Jan van de Winkel, Steen Lisby</i>
5:00 PM	Refreshments	
5:30 PM	Close	

Forward Looking Statement

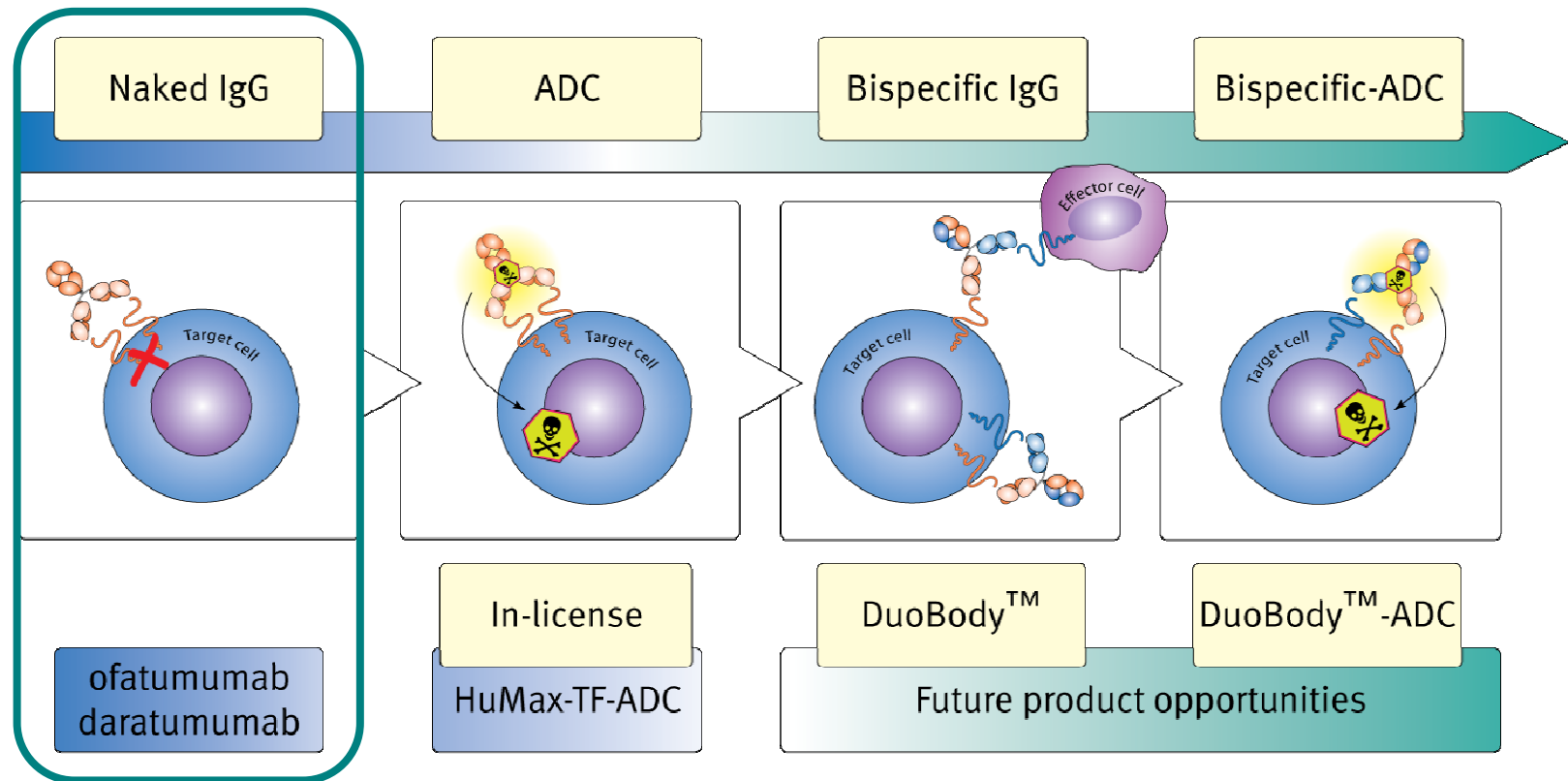
This presentation contains forward looking statements. The words “believe”, “expect”, “anticipate”, “intend” and “plan” and similar expressions identify forward looking statements. All statements other than statements of historical facts included in this presentation, including, without limitation, those 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.

2011 Objectives

Managing Our Priorities

Priority	Goal	Current Progress
Maximize value of ofatumumab	• Report Ph II CLL & DLBCL data • Report Ph I/II RA subQ data • Start Ph II MS subQ trial • Launch & reimbursement in new countries	✓ DLBCL data reported ✓ Presented at EULAR in May ✓ Study initiated ✓ Launched in 22 countries
Evaluate opportunities for zalutumumab	• Partnership progress • Reduce cash investment	Decision to wind down program Spend mostly complete in 2011
Daratumumab	• Report Ph I/II study data • Initiate Ph I/II combination trial	✓ Clinical data presented at ASH Trial planning in progress, 1 st patient anticipated in early 2012
Expand pipeline	• Announce new IND candidate	✓ Announced HuMax[®]-CD74-ADC
Enter new strategic collaboration	• Sign new partnership agreement	✓ Entered 2nd ADC agreement with Seattle Genetics
Optimize ways to advance next generation technologies	• Advance DuoBody[™] • Enter new collaborations	✓ Large scale manufacturing. validation
Promote sale of manufacturing facility	• Progress sale	Fair value reduced to USD 58 M Sale moved to 2012
Manage and control cash burn	• Meet or beat 2011 guidance	✓ Guidance for continuing operations improved in Q2 & Q3

Genmab Product Innovation

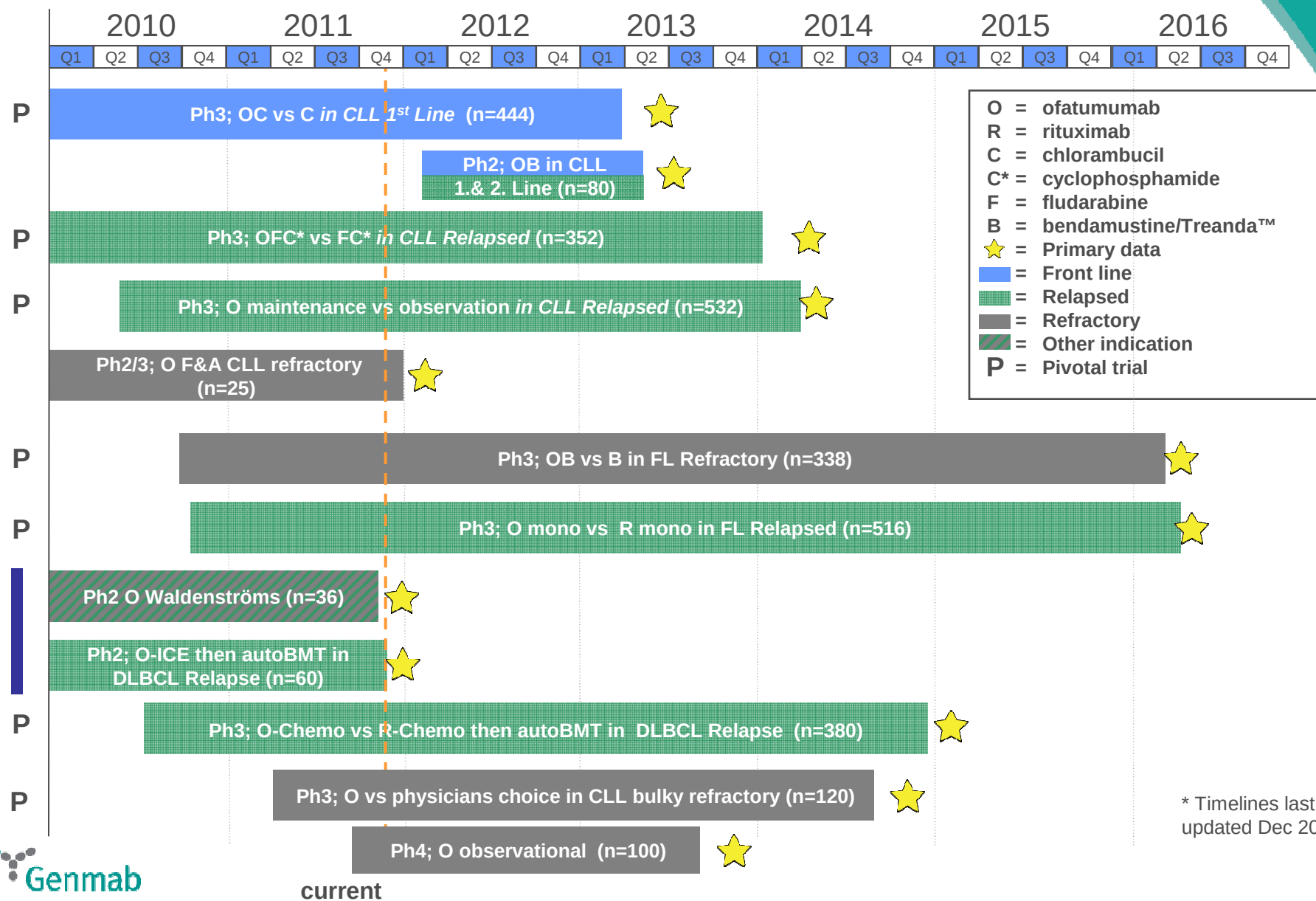


Arzerra® (ofatumumab)

- Fully human antibody
- Approved in US & EU for patients with CLL that does not respond to current treatments (fludarabine & alemtuzumab)
- Targets CD20 molecule on B-cells which can become cancerous
- Effectively engages immune system
- Blockbuster potential in oncology; potential in autoimmune diseases such as MS
- Successful collaboration with GSK since 2006
- Sales in 2010: GBP 31 M
- Sales in first 9 months 2011: GBP 31.8 M

Ofatumumab Oncology Clinical Trials

Timeline* to Primary Data – December 2011



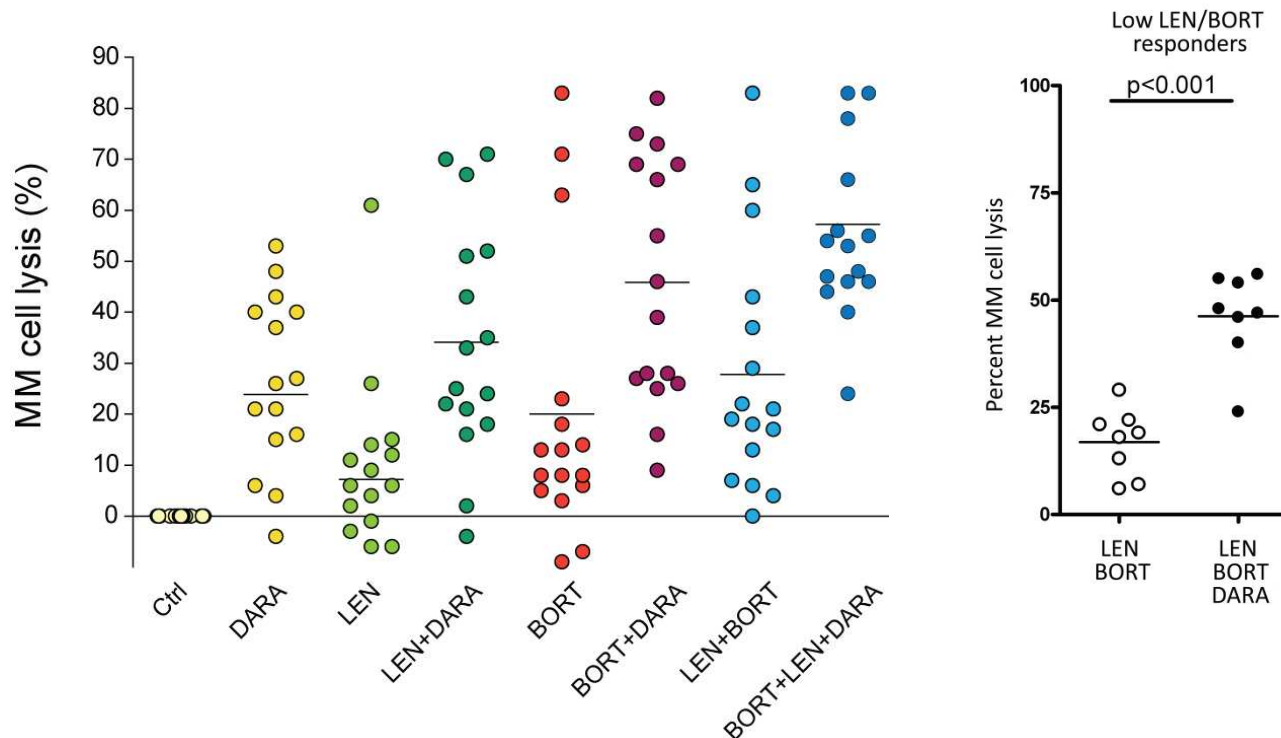
Daratumumab (HuMax[®]-CD38)

- First-in-class antibody with potential in Multiple Myeloma (MM), DLBCL, FL, Mantle Cell lymphoma, ALL and AML
- Fully human, high affinity antibody that targets CD38, a molecule highly expressed on MM
- Broad-spectrum killing activity in pre-clinical settings
- Inhibits tumor growth in animal models; active at very low doses
- Enhances cell killing in combination with current treatments (Revlimid & Velcade) in pre-clinical settings
- Genmab owns worldwide rights
- Daratumumab targets a potential MM market of >\$3.5 B

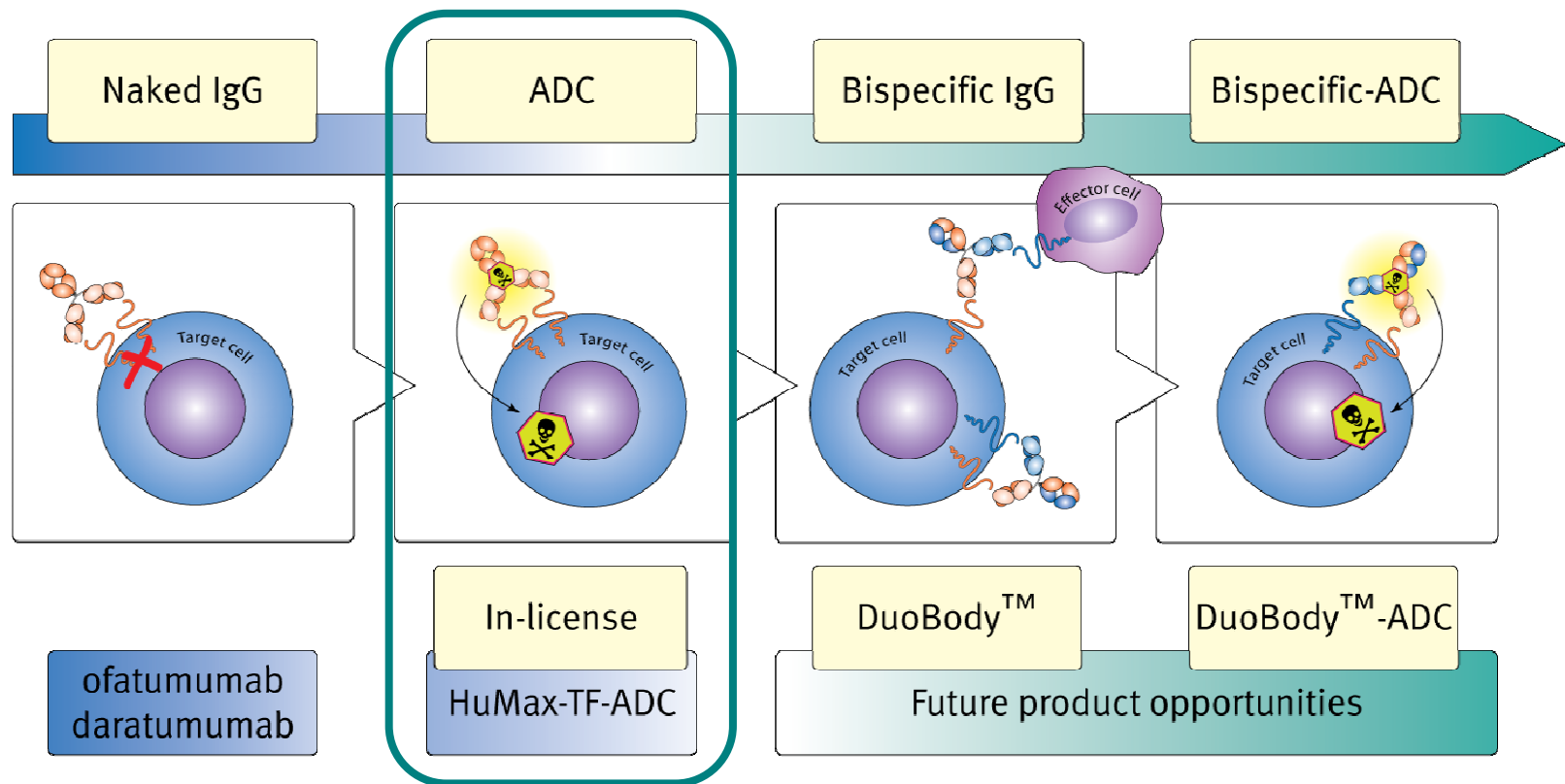
Daratumumab

Combination Therapy with Lenalidomide/Bortezomib

- Synergistic cell killing of primary MM tumor cells
- Induces killing when LEN/BORT alone are ineffective



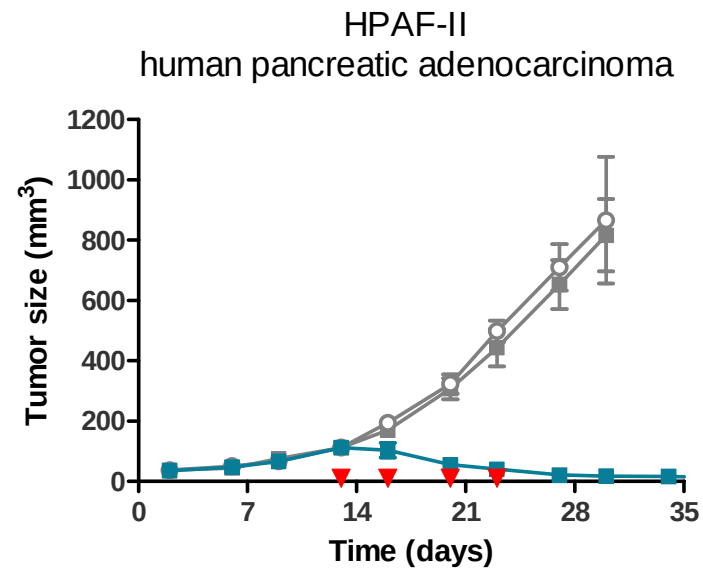
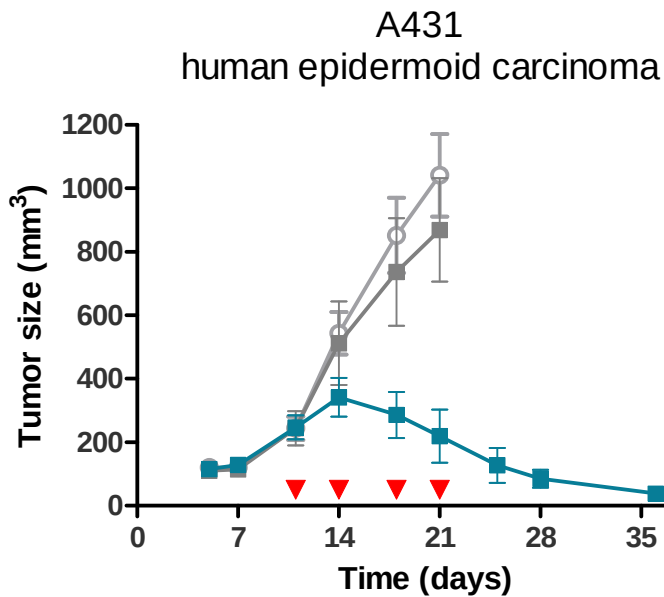
Genmab Product Innovation



HuMax[®]-TF-ADC

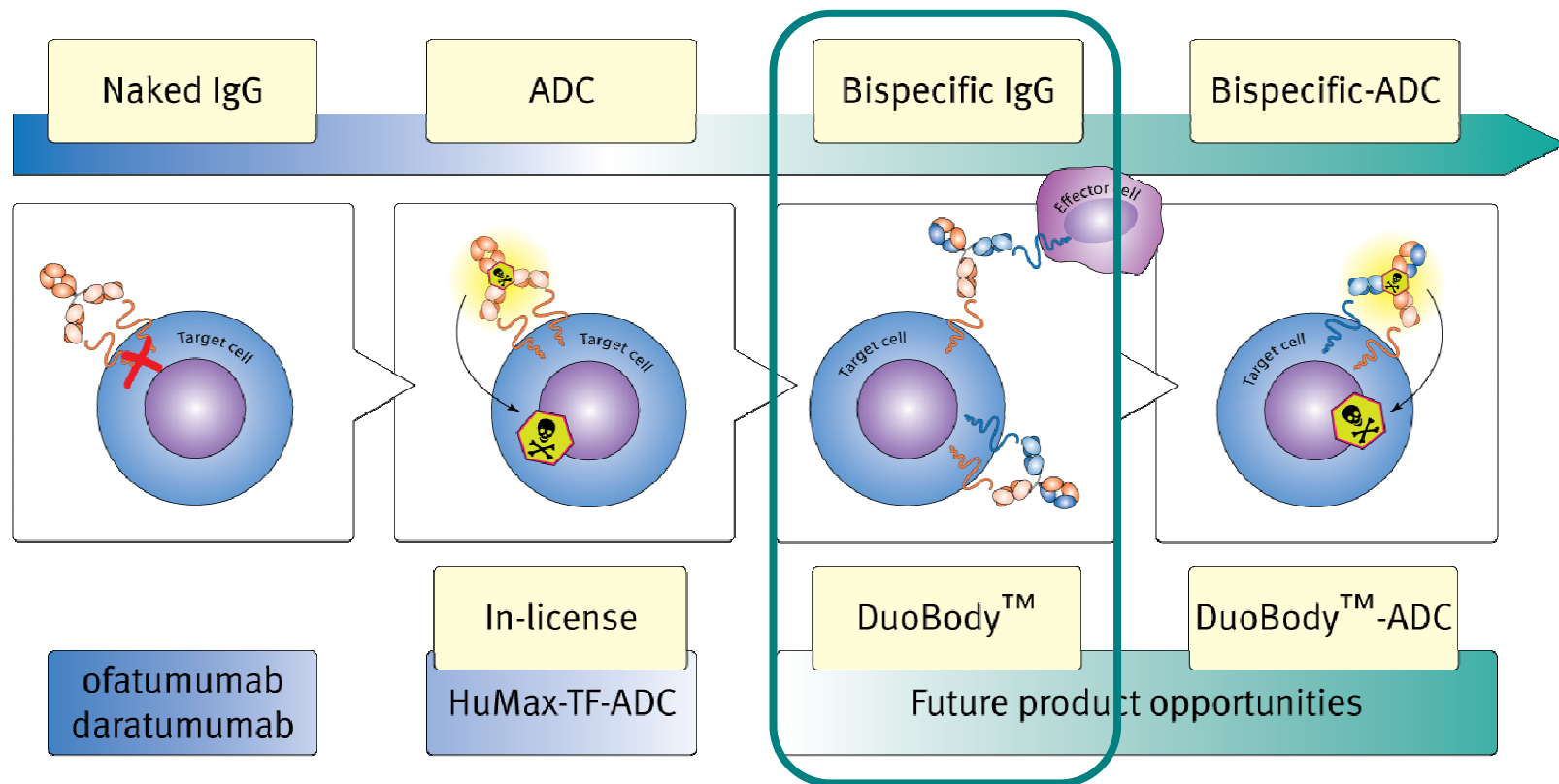
In vivo Efficacy

- HuMax-TF-ADC efficiently inhibits tumor outgrowth in different *in vivo* xenograft models
- IND preparation ongoing



- Isotype control
- Isotype control ADC
- HuMax-TF-ADC
- ▼ Treatment

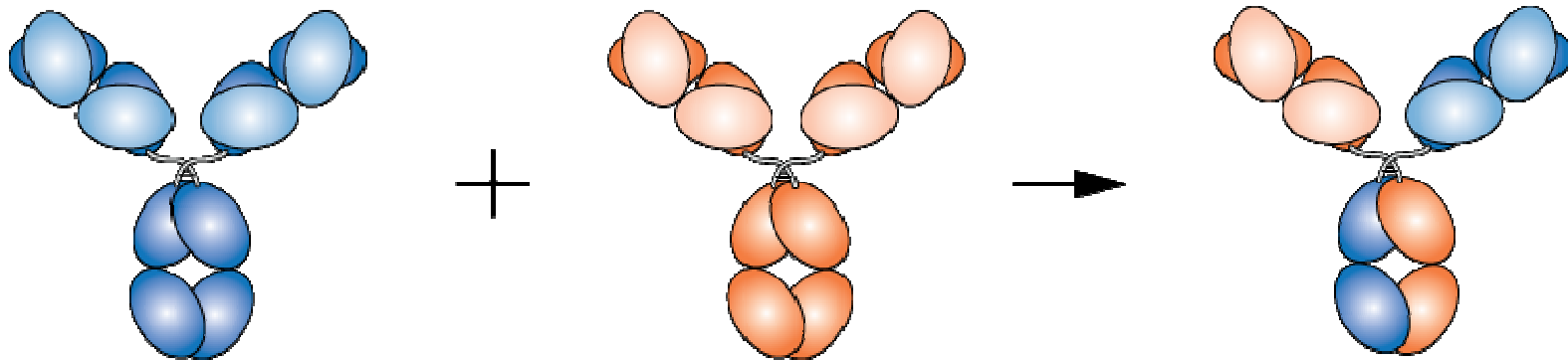
Genmab Product Innovation



Therapeutic Bispecific Antibodies

Controlled Fab-Arm Exchange

- Controlled Fab-arm exchange by:
 - Limited amino acid modifications
 - Controlled exchange permissive conditions

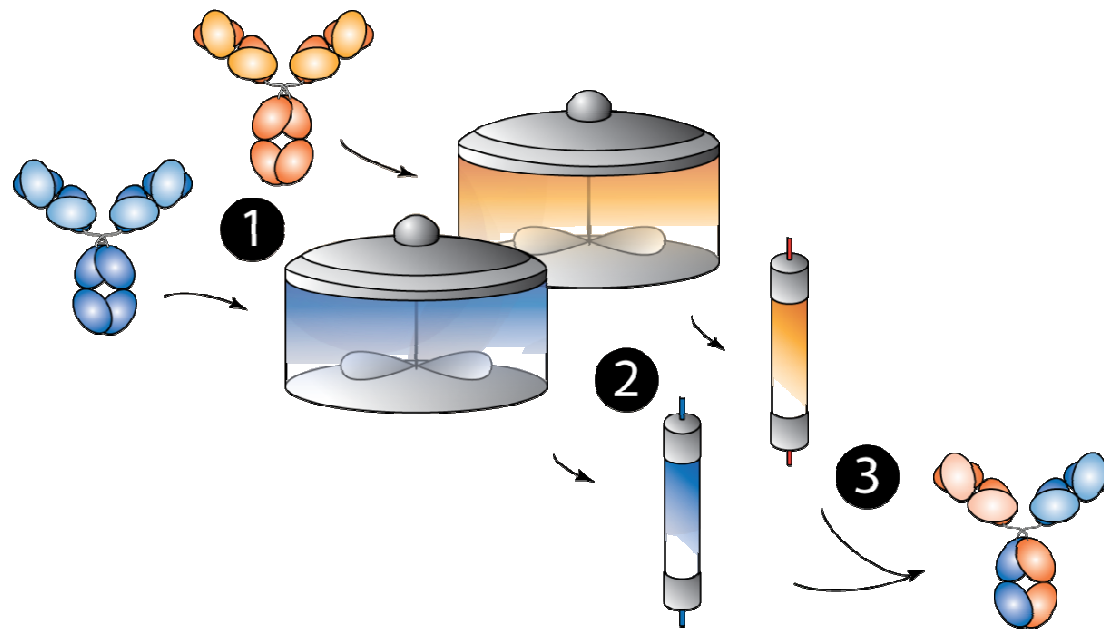


DuoBody™ Platform

Simple Post-Production Process

Manufacturing based on standard unit operations for IgG1

- Separate expression of two parental IgG1 antibodies
- Purification using standard IgG1 downstream processes
- Efficient generation bispecific IgG1 Ab using disposable technologies at required scale



DuoBody™ Platform

Large Scale Manufacturing: Excellent Scalability

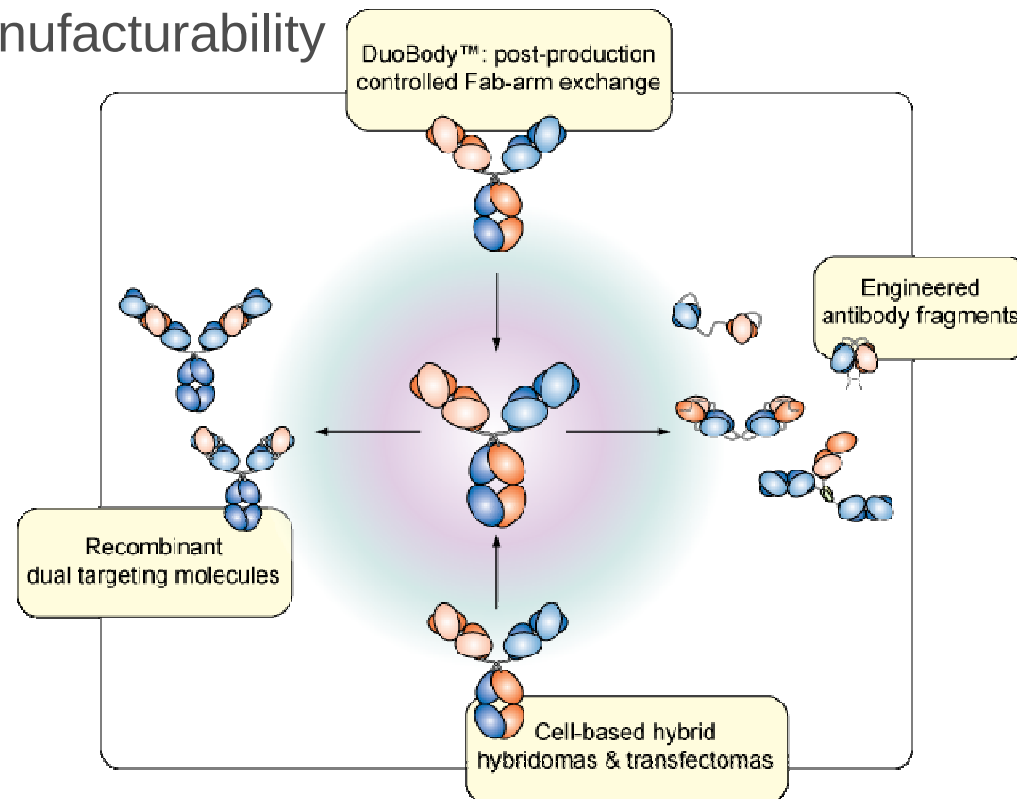
- Robust manufacturability
- DuoBody™ platform is suitable for large scale manufacturing
 - 0.5 kg bispecific antibody batch was produced (25 liter at 20 g/L)
 - Excellent antibody quality
 - No optimization of bench scale protocol required



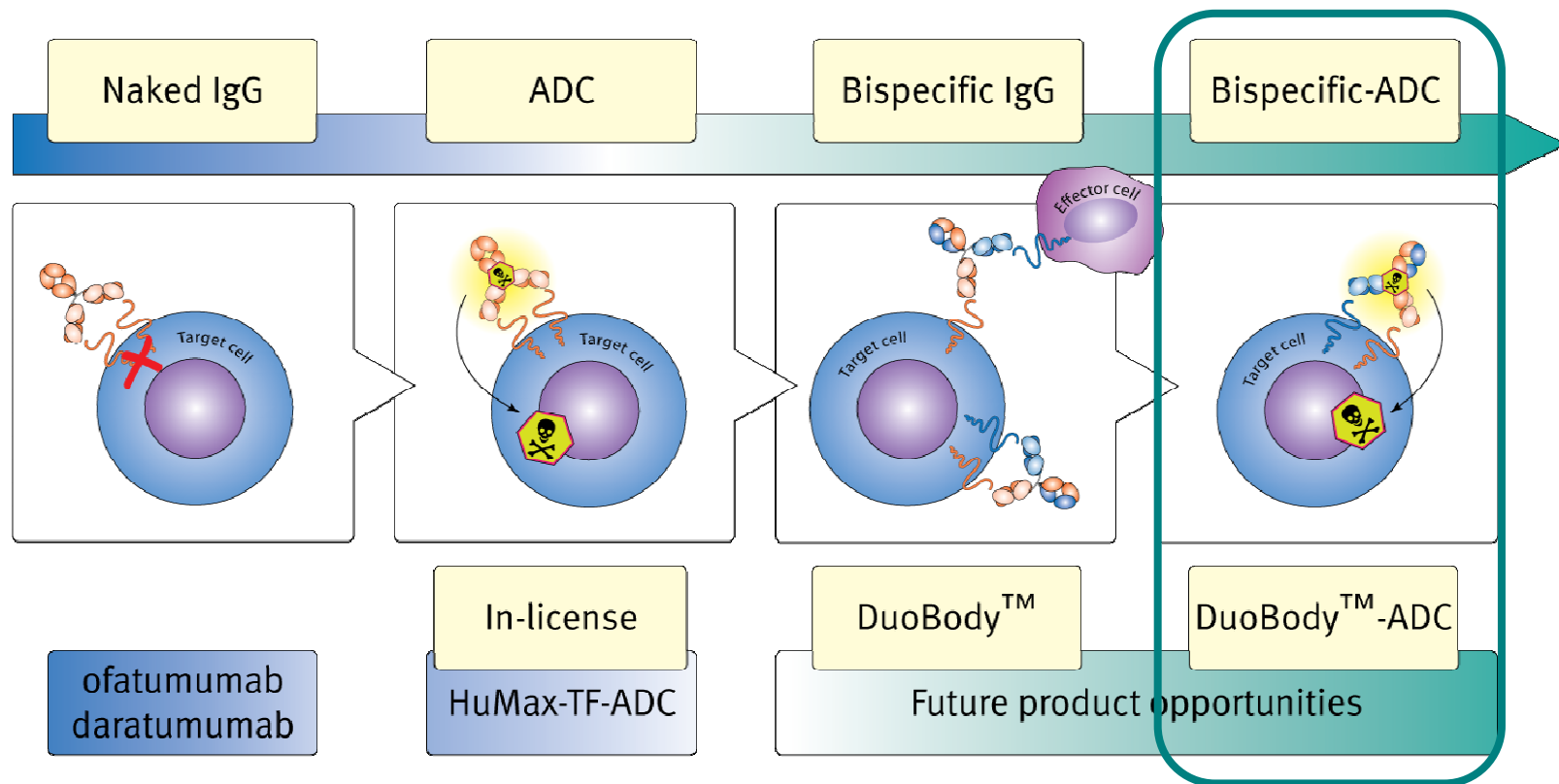
Bispecific Antibody Therapy

Competitor Platforms

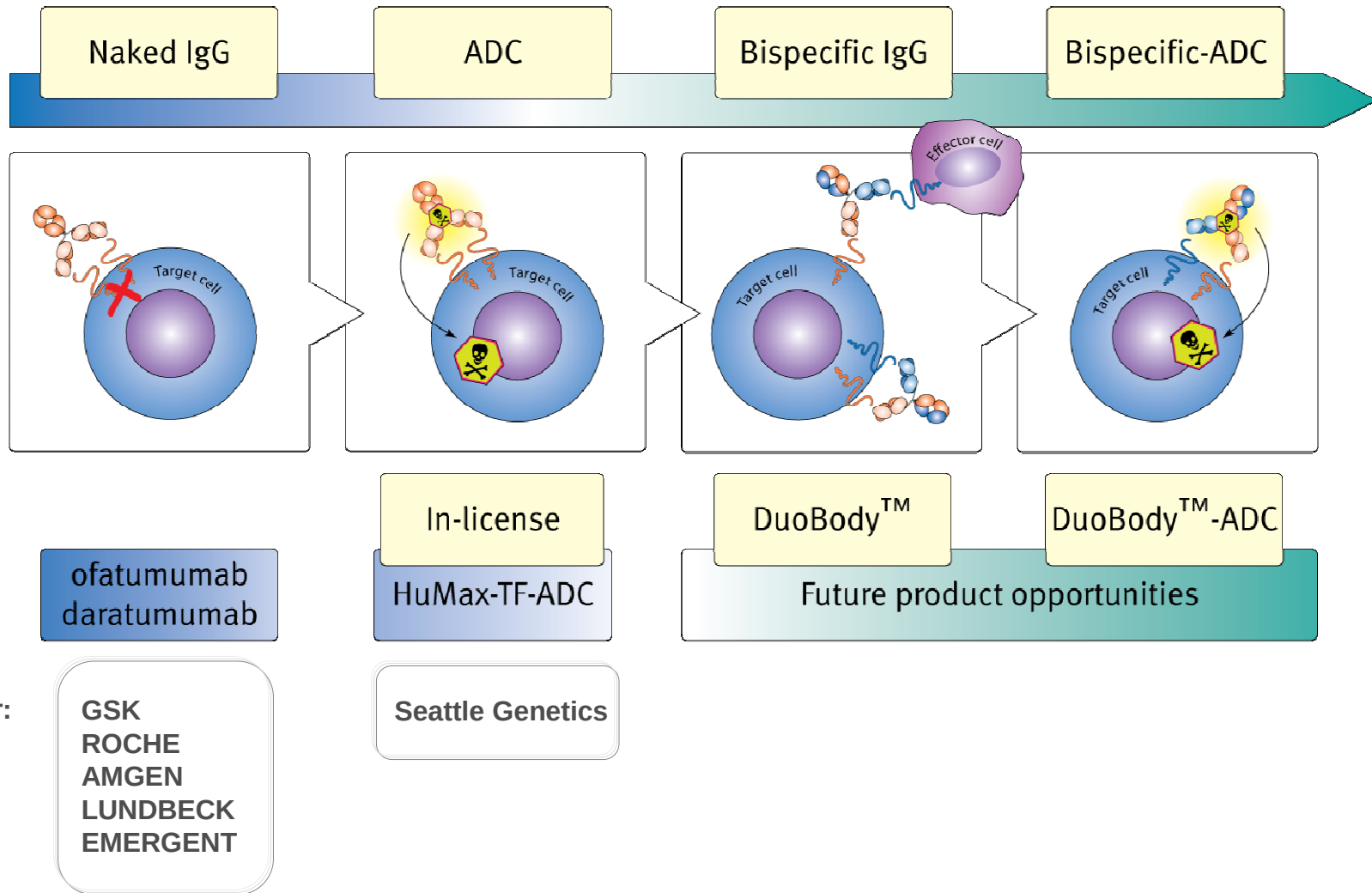
- DuoBody™ platform distinguished from competitor platforms by retaining a regular IgG structure and combining
 - Proper *in vivo* half-life
 - Fc-effector functions
 - Good manufacturability



Genmab Product Innovation



Driving Value Through Partnerships



Ofatumumab in Relapsed or Refractory Aggressive B-Cell Lymphoma

Presenter: Anton Hagenbeek, M.D., Ph.D.*

Academic Medical Center, Dept. Hematology,

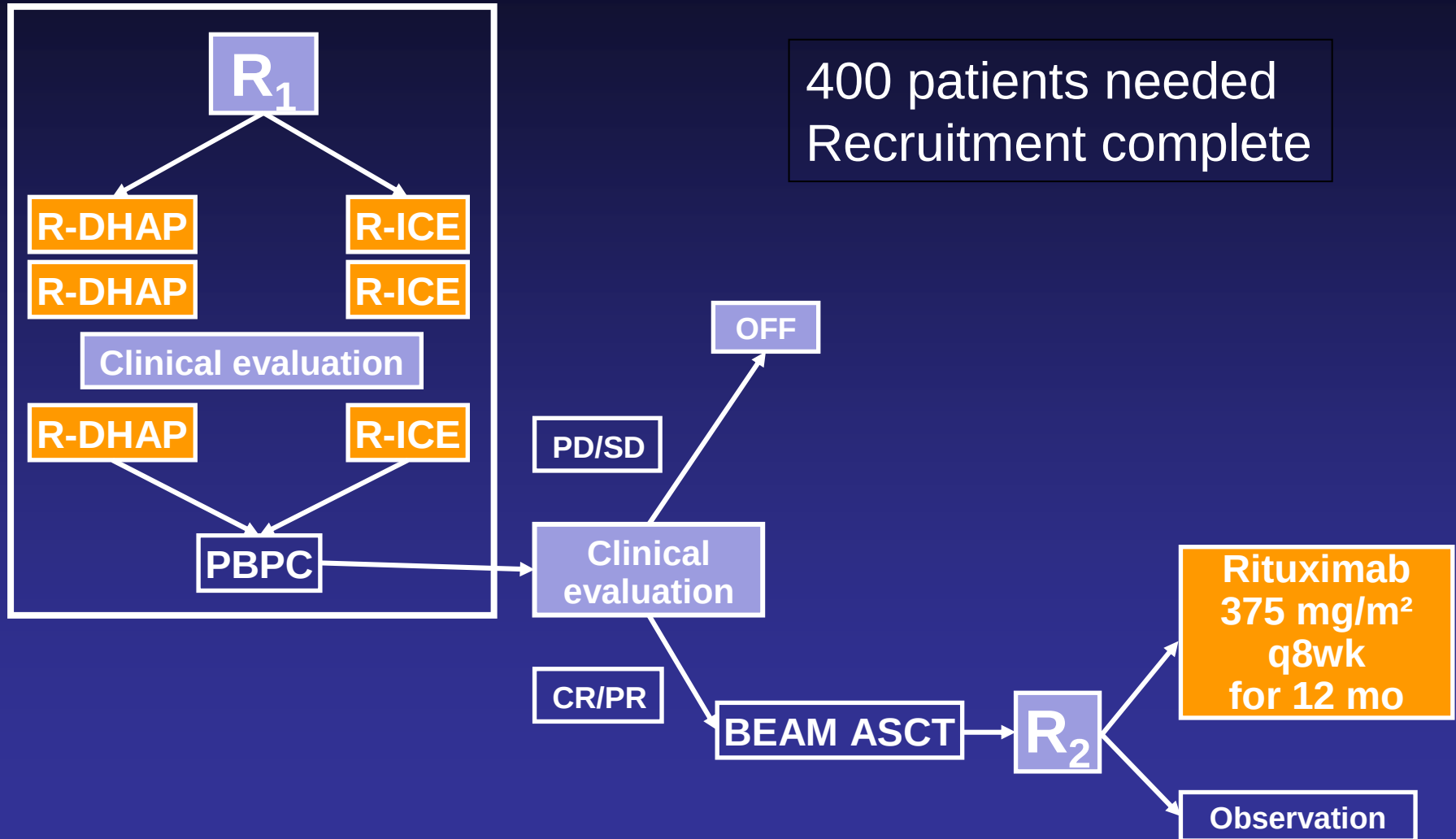
Amsterdam, the Netherlands

* Coordinating Principle Investigator, ORCHARRD

Background

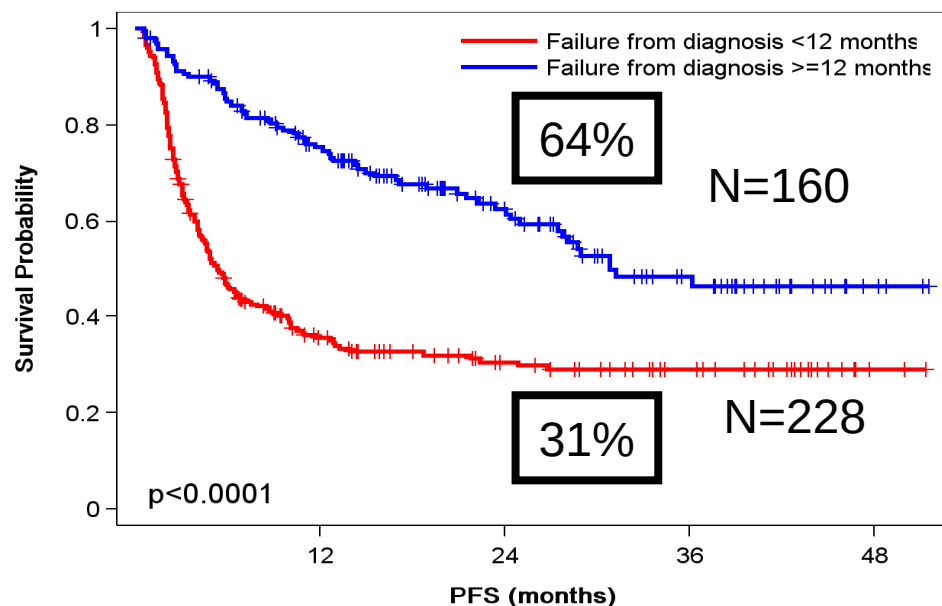
- Inclusion of rituximab (R) in first-line therapy for diffuse large B-cell lymphoma (DLBCL) leads to improved outcomes
- Relapsed or refractory disease following R with cyclophosphamide, doxorubicin, vincristine and prednisone (R-CHOP) carries a poor prognosis
- Response rates with R + chemotherapy (ifosfamide, carboplatin and etoposide [ICE] or dexamethasone, cytarabine and cisplatin [DHAP], typically) following first-line R + chemotherapy are lower than following chemotherapy alone, and more closely resemble second-line response rates in the pre-rituximab era
- The CORAL study established overall equivalence of R+ICE and R+DHAP in the treatment of relapsed or refractory DLBCL

CORAL Study: R-ICE versus R-DHAP followed by ASCT $\pm$ maintenance

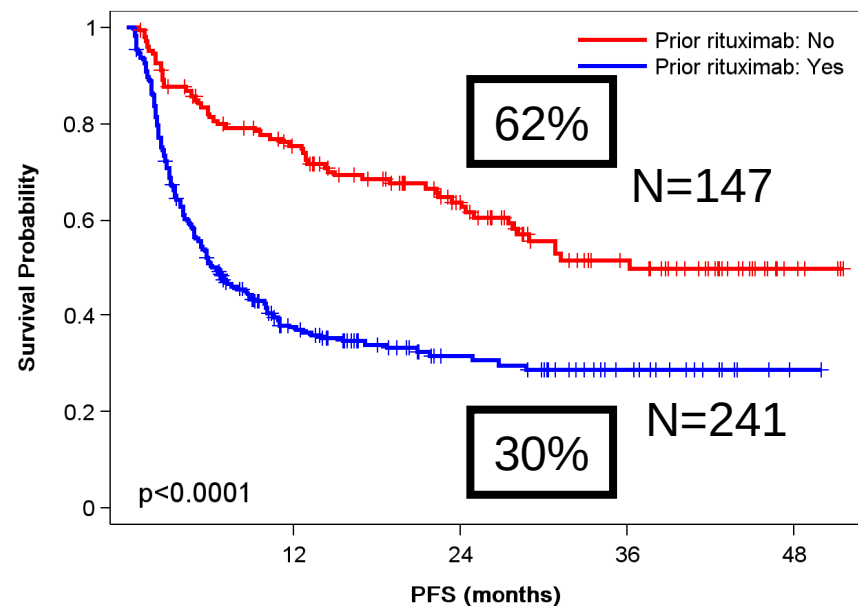


Progression-free survival

Progression-free survival according to failure from diagnosis (induction ITT)



Progression-free survival according to prior rituximab (induction ITT)



Gisselbrecht et al. J Clin Oncol 2010, 28, 4184.

Rationale to explore ofatumumab in the treatment of DLBCL

- Ofatumumab, a human CD20 antibody that targets the small-loop epitope of CD20, may help to improve the overall response rates (ORR) in relapsed or refractory DLBCL

Ofatumumab as monotherapy in DLBCL

- Ofatumumab monotherapy in patients with relapse after CR or disease progression after PR who were ineligible to ASCT or relapsed/progressive disease following ASCT
- Treatment schedule of ofatumumab was 300 mg followed by 7 weekly doses of 1000 mg for a total of 8 week dosing period

• N	81
• Median age	68 years (22-87)
• Stage III/IV	64 (79%)
• Number of prior therapies, Median (range)	3 (1-6)
• Prior ASCT	25 (31%)
• Prior rituximab therapies	78 (96%)
• ≥ 2 prior courses of rtx-containing therapy	44 (54%)

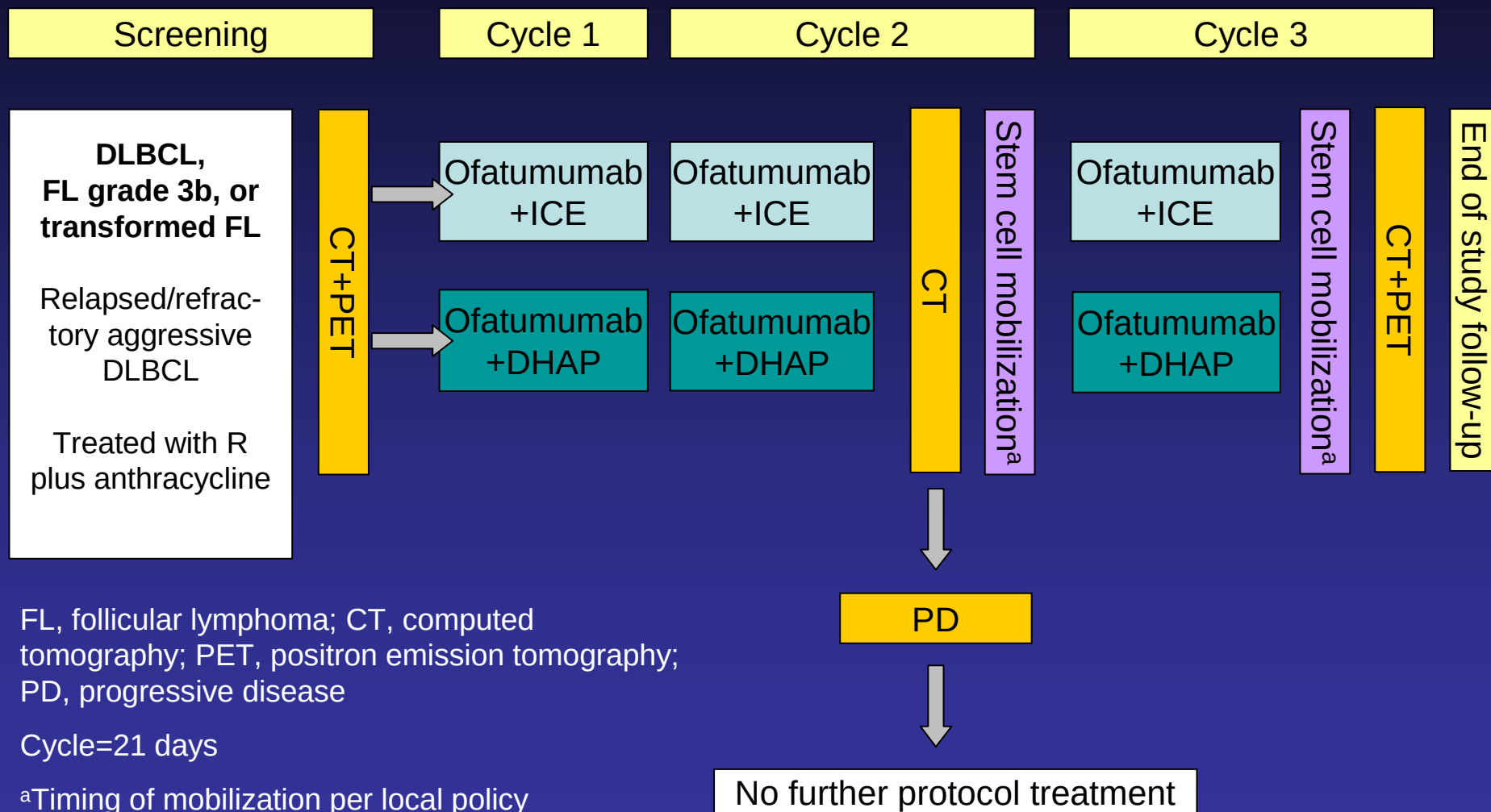
Ofatumumab as monotherapy shows activity in relapsed refractory DLBCL

- Overall response rate was 11% (3 CR and 6 PR)
- In patients with >6 months response to last treatment, a 22% ORR was observed
- 7 of the 9 responders previously had failed rituximab-containing therapy
- Median duration of response was 6.9 months

ASH Abstract #957
**A Phase II Study of Ofatumumab in Combination with
ICE or DHAP Chemotherapy in Relapsed or
Refractory Aggressive B-Cell Lymphoma Prior to
High-Dose Therapy with Autologous Stem Cell
Rescue (ASCR)**

Matthew J. Matasar, Maria Alma Rodriguez, Myron S. Czuczman,
Michael Fennessy, Thomas C. Shea, Gary Spitzer, Izidore S. Lossos,
Mohamed A. Kharfan-Dabaja, Robin Joyce, Luis Fayad, Qiming Liao,
Klaus Edvardsen, Steen Lisby and Craig H. Moskowitz

Study design



Study objectives and statistical design

Primary objective

- ORR of ofatumumab in combination with ICE or DHAP chemotherapy

Secondary objectives

- Complete response (CR) rate (defined by negative fluorodeoxyglucose [^{18}F FDG]-PET scan)
- Mobilization of $\geq 2 \times 10^6$ CD34+ cells/kg
- Safety and tolerability
- Progression-free survival (PFS), overall survival (OS)

Statistical design

- Multicenter, phase II trial
- Chemotherapy (ICE or DHAP) selected a priori per individual center preference
- Target ORR=60%; N=60 to permit an evaluable N=54

Eligibility criteria

Key inclusion criteria

- CD20+ DLBCL, FL grade 3b or transformed FL
- Refractory or relapsed disease: tissue confirmation required for relapsed disease, recommended for refractory disease
- First-line therapy with R + anthracycline-based chemotherapy
- Measurable ^{18}F FDG-PET avid disease
- Eastern Cooperative Oncology Group (ECOG) performance status of 0 to 2
- Eligible for high-dose therapy with autologous stem cell rescue (HDT/ASCR)

Key exclusion criteria

- Hepatitis B or C viremia, HIV infection
- Central nervous system (CNS) or leptomeningeal disease
- Major comorbidity precluding participation or transplantation

Chemotherapy regimens

- 21-day cycles
- Ofatumumab on cycle 1, days 1 and 8, and cycles 2 and 3, day 1
 - Cycle 1, day 1 dose 300 mg initially, amended to 1000 mg after 21 patients
 - Subsequent doses 1000 mg
- ICE
 - Etoposide 100 mg/m² on days 1–3
 - Carboplatin area under the curve (AUC) 5 (800 mg maximum) on day 2
 - Ifosfamide + mesna 5 g/m²/24 h on day 2
- DHAP
 - Dexamethasone 40 mg (oral or intravenously) on days 1–4
 - Cisplatin 100 mg/m²/24 h on day 1
 - Cytarabine 2 g/m² every 12 hours (2 doses) on day 2
- Dose reductions/adjustments were not permitted; regimen could be switched for non-hematologic toxicity

Demographics and baseline characteristics

	O+DHAP n=26	O+ICE n=35	Total N=61
Median age, years (range)	54 (20–66)	52 (27–79)	53 (20–79)
Age $\geq$ 60 years, n (%)	8 (31)	8 (23)	16 (26)
Male, n (%)	15 (58)	20 (57)	35 (57)
White, n (%)	22 (85)	33 (94)	55 (91)
LDH (> ULN), n (%)	16 (62)	20 (57)	36 (59)

Patient characteristics

	O+DHAP n=26	O+ICE n=35	Total N=61
Histology, n (%)			
DLBCL	21 (81)	26 (74)	47 (77)
Grade 3b	0	2 (6)	2 (3)
Transformed	5 (19)	7 (20)	12 (20)
ECOG PS, n (%)			
0/1	24 (92)	32 (91)	56 (92)
2	2 (8)	3 (9)	5 (8)
sAAIPI, n (%)			
0/1	13 (50)	19 (54)	32 (52)
2/3	13 (50)	16 (46)	29 (48)

Best response from first-line treatment

	O+DHAP n=26	O+ICE n=35	Total N=61
Relapsed, n (%)	13 (50)	17 (49)	30 (49)
CR >12 months	4 (15)	8 (23)	12 (20)
CR ≤12 months	9 (35)	9 (26)	18 (30)
Refractory, n (%)	13 (50)	16 (46)	29 (48)
PR	6 (22)	9 (26)	15 (25)
SD	2 (8)	2 (6)	4 (7)
PD	5 (19)	5 (14)	10 (16)
Unknown, n (%)	0	2 (6)	2 (3)

Best response from first-line treatment

	O+DHAP n=26	O+ICE n=35	Total N=61
Relapsed, n (%)	13 (50)	17 (49)	30 (49)
CR >12 months	4 (15)	8 (23)	12 (20)
CR ≤12 months	9 (35)	9 (26)	18 (30)
Refractory, n (%)	13 (50)	16 (46)	29 (48)
PR	6 (22)	9 (26)	15 (25)
SD	2 (8)	2 (6)	4 (7)
PD	5 (19)	5 (14)	10 (16)
Unknown, n (%)	0	2 (6)	2 (3)

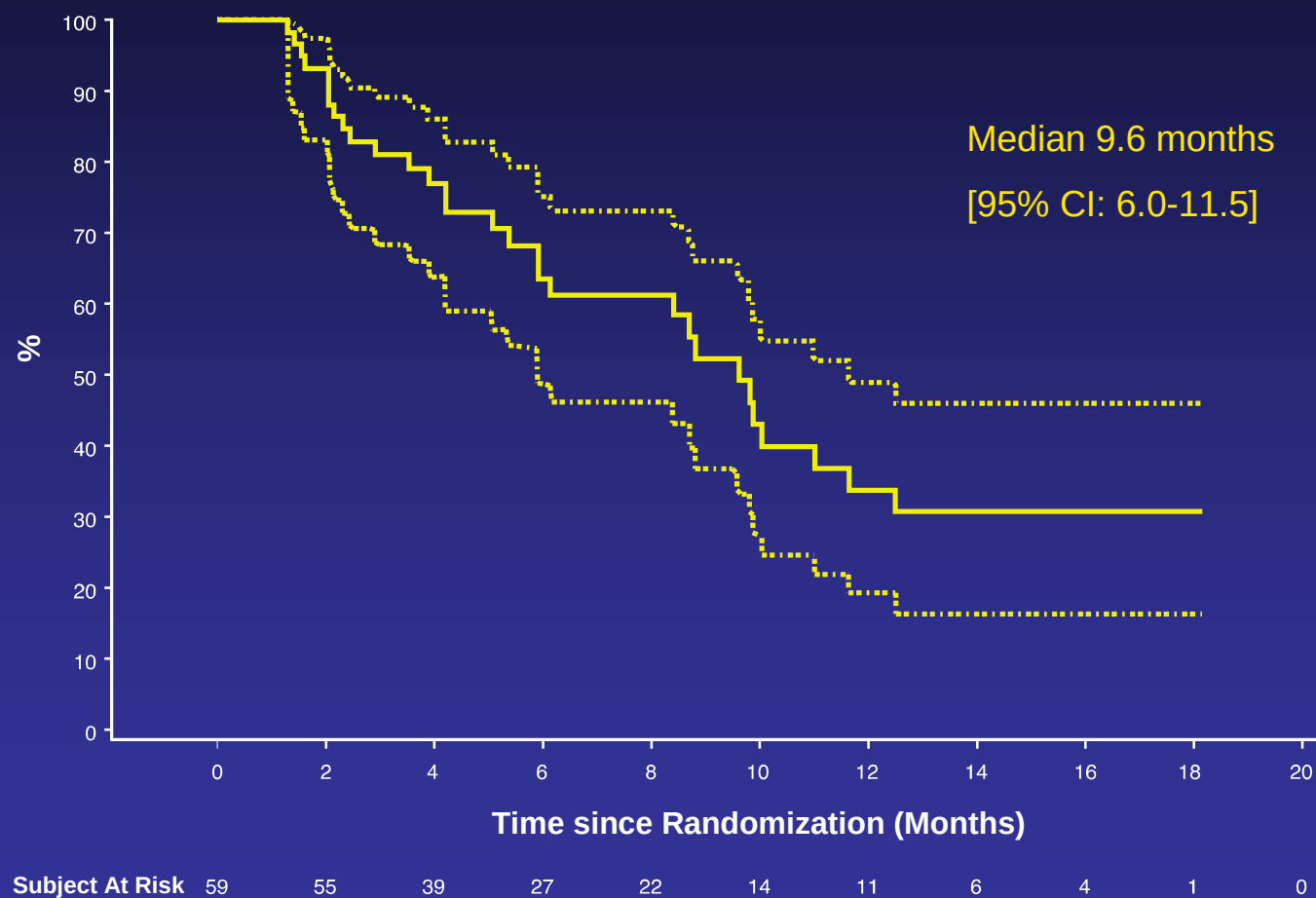
Response by regimen

	O+DHAP n=26	O+ICE n=33	Total N=59
CR, n (%)	11 (42)	11 (33)	22 (37)
PR, n (%)	7 (27)	7 (21)	14 (24)
Non-response, n (%)	8 (31)	15 (45)	23 (39)
ORR (CR + PR), n (%)	18 (69)	18 (55)	36 (61)

Response by sAAIPI

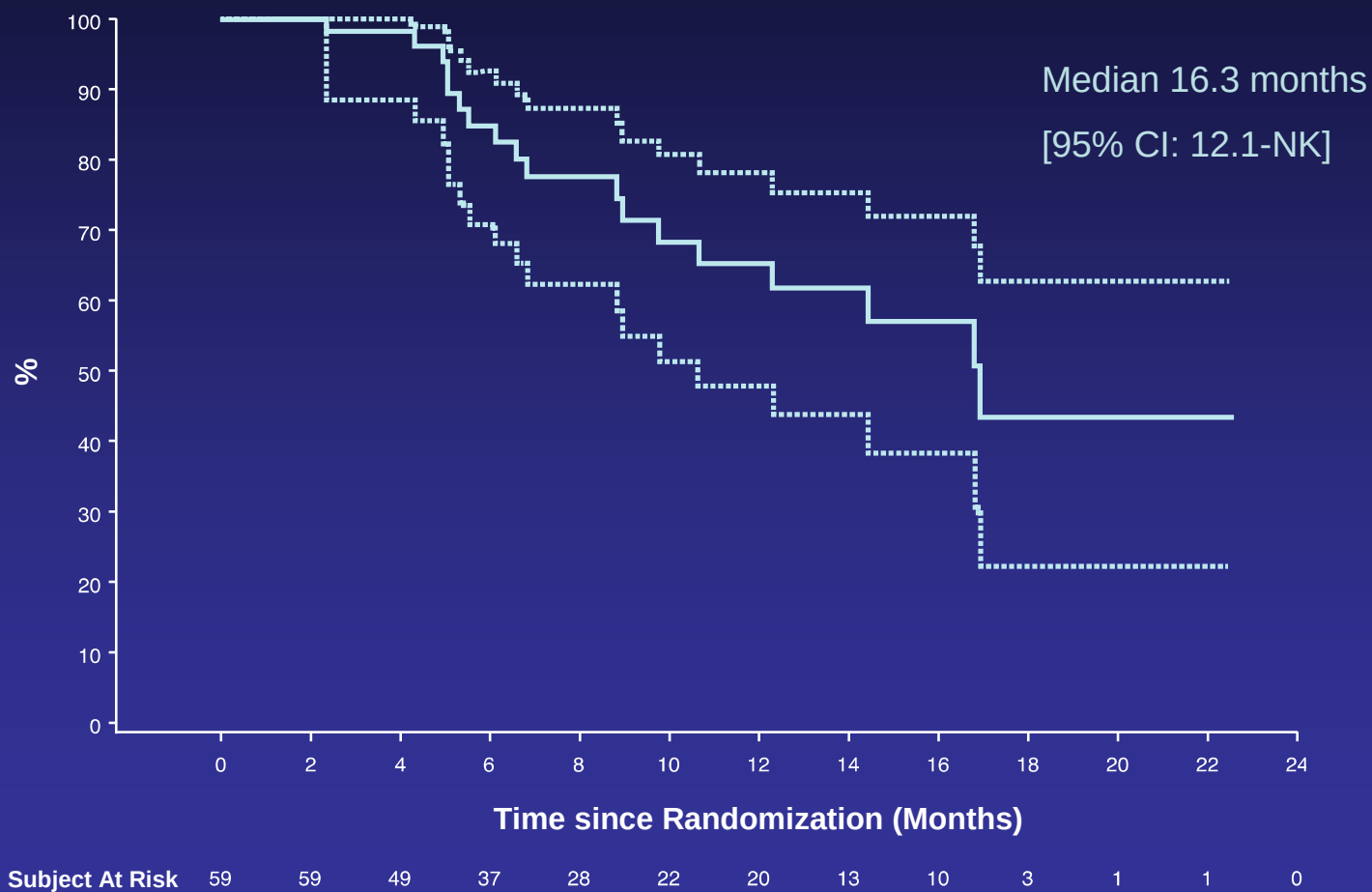
	sAAIPI 0/1 n=30	sAAIPI 2/3 n=29	Total N=59
CR, n (%)	13 (43)	9 (31)	22 (37)
PR, n (%)	6 (20)	8 (28)	14 (24)
Non-response, n (%)	11 (37)	12 (41)	23 (39)
ORR (CR + PR), n (%)	19 (63)	17 (59)	36 (61)

Progression-free survival



CI, confidence interval

Overall survival



NK, not known

Stem cell mobilization

	O+DHAP n=26	O+ICE n=33	Total N=59
Underwent PBSC mobilization, n	23	22	45
Mobilized $\geq 2 \times 10^6$ CD34+ cells/kg, n (%)	23 (100)	20 (91)	43 (96)
CD34+ cells collected			
Median	$6.5 \times 10^6/\text{kg}$	$5 \times 10^6/\text{kg}$	$5.8 \times 10^6/\text{kg}$
Range	3–31.6	0.4–27.4	0.4–31.6

Adverse events and deaths

Adverse event, n (%)	O+DHAP n=26	O+ICE n=35	Total N=61
Anemia	14 (54)	16 (46)	30 ^a (49)
Thrombocytopenia	20 (77)	19 (54)	39 ^b (64)
Febrile neutropenia	8 (31)	1 (3)	9 ^c (15)
Infection	9 (35)	6 (17)	15 ^d (25)
Renal failure	4 (15)	2 (6)	6 ^e (10)
Increased creatinin	11 (42)	3 (9)	14 ^e (23)
Infusion reaction ^f			
First infusion	18 (69)	20 (57)	38 ^g (62)
Subsequent infusion	11 (42)	19 (54)	30 ^h (49)

- 47/61 patients (77%) experienced a grade 3/4 AE
- 3 patients discontinued study drug due to AEs
- 1 patient died 18 days from last dose due to respiratory failure
- 19 additional deaths occurred during post study follow-up

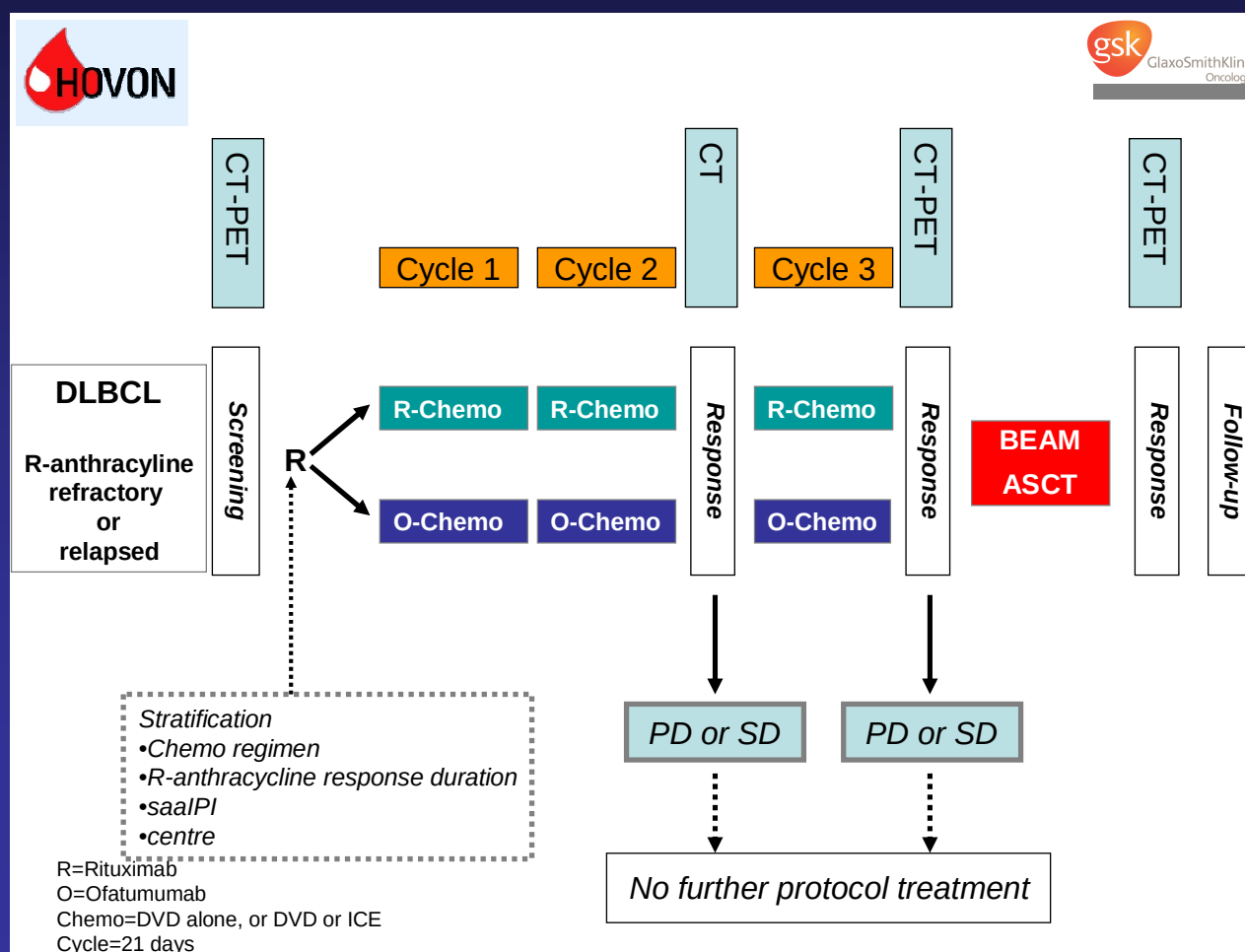
^aFor anemia, 22 (36%) were grade 3/4. ^bFor thrombocytopenia, 36 (59%) were grade 3/4. ^cFor febrile neutropenia, 8 (13%) were grade 3/4. ^dFor infection, 6 (10%) were grade 3/4. ^eFor renal failure, 4 (13%) were grade 3/4. ^fSymptoms associated with infusion reactions occurring within 24 h of infusion. ^gFor first infusion, 8 (13%) were grade 3/4. ^hFor subsequent infusions, 5 (8%) were grade 3/4.

Summary

- The combination of ofatumumab with ICE or DHAP shows promising activity, with an ORR of 61% in a high-risk population
- No unexpected toxicity was seen, and stem cell mobilization was not adversely affected
- ORR of 59% in high-risk patients (sAAIPI 2 or 3) is promising
- Requires confirmation from prospective phase III study

Study design – Phase III study ORCHARRD

Ofatumumab Versus Rituximab Salvage Chemoimmunotherapy
Followed by Autologous Stem Cell Transplant in Relapsed or Refractory
Diffuse Large B Cell Lymphoma



Ofatumumab Phase III study - ORCHARRD

Ofatumumab Versus Rituximab Salvage Chemoimmunotherapy
Followed by Autologous Stem Cell Transplant in Relapsed or Refractory
Diffuse Large B Cell Lymphoma

Estimated Enrollment: 380
Study Start Date: March 2010
Estimated Study Completion Date: December 2017
Estimated Primary Completion Date: December 2014
(Final data collection date for primary outcome measure)

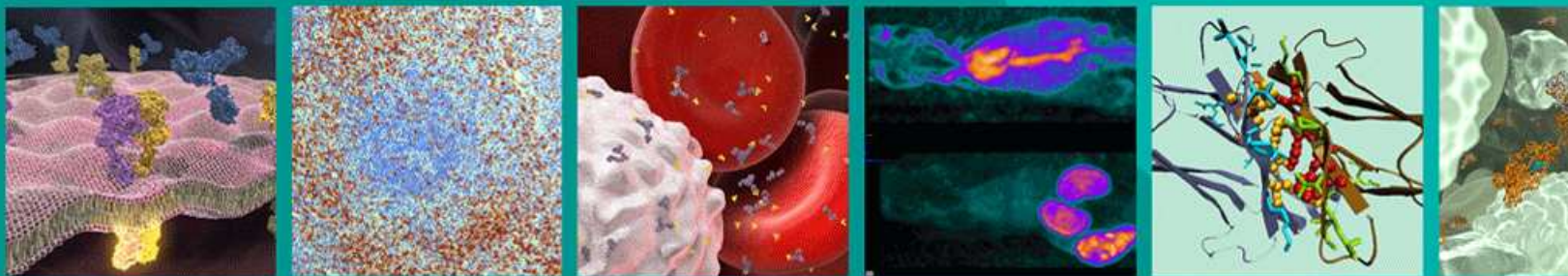
Interim futility and safety analysis after 70 patients in each arm



A Phase II Trial of Ofatumumab in Subjects With Waldenström's Macroglobulinemia

ASH abstr # 3701

Presenter: Steen Lisby, M.D., Ph.D.,
Sr. Medical Director, Genmab



Introduction

- Waldenström's macroglobulinemia (WM) is an indolent B-cell non-Hodgkin's lymphoplasmacytic lymphoma characterized by variable or low CD20 expression and production of a monoclonal IgM paraprotein
- Complications of WM include hyperviscosity syndrome, autoimmune hemolysis, and renal insufficiency
- Lower response described in patients with high monoclonal IgM*
- Ofatumumab is a unique monoclonal antibody that targets a distinct small loop epitope on the CD20 molecule
- This study was designed to investigate the clinical efficacy and safety of single-agent ofatumumab in WM

Methods

Patient population

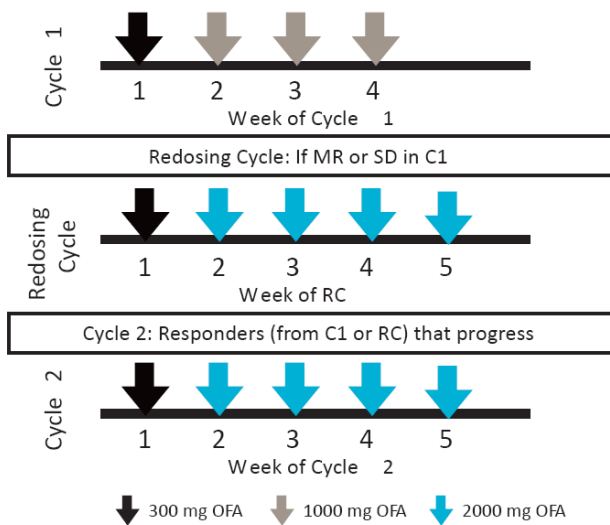
- Patients aged ≥ 18 years, with untreated or previously treated WM requiring therapy by 2nd International Workshop on WM criteria²
- CD20 expression confirmed by bone marrow immunohistochemistry or flow cytometric analysis
- Eastern Cooperative Oncology Group performance status of 0, 1, or 2
- IgM paraprotein level > 1000 mg/dL

Study design

- Open-label, multicenter, single-arm, phase II trial conducted in the United States
- Two treatment groups received up to 3 cycles of therapy
- After safety was confirmed in the first 15 patients treated at 1000 mg, dosing was adjusted to the 2000-mg dose approved in chronic lymphocytic leukemia (CLL) due to the similar low expression of CD20 in CLL and WM

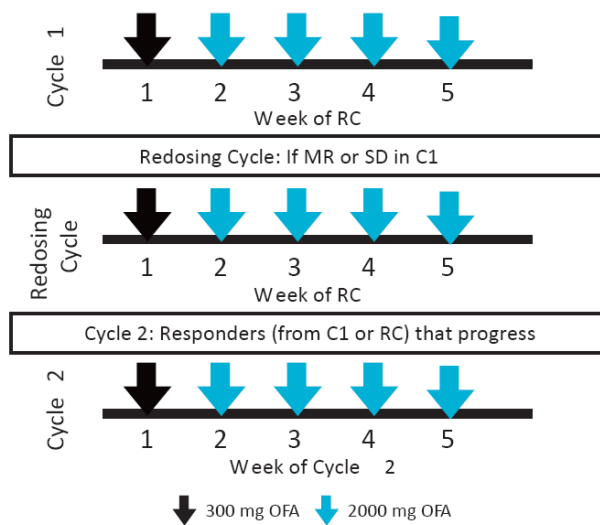
Study design overview

Figure 1. Treatment Group A



MR, minor response; SD, stable disease; C1, cycle 1; RC, redosing cycle; OFA, ofatumumab

Figure 2. Treatment Group B



Endpoint evaluations

- Primary endpoint
 - ORR, assessed by 2nd International Workshop on WM criteria
- Secondary endpoints
 - Complete response (CR), partial response (PR; $\geq 50\%$ reduction in IgM) and MR (25%–49% reduction in IgM) rates
 - Progression-free survival, overall survival, and duration of response
 - Incidence of IgM flare (defined by an increase $>25\%$ from baseline and associated with subsequent response to treatment)
 - Safety and toxicity; adverse events (AEs) were graded according to the National Cancer Institute Common Terminology Criteria for Adverse Events v3.0

Results

Patient characteristics (n=37 subjects)

Table 1. Patient characteristics			
	TGA n=15	TGB n=22	Total n=37
Median age, years (range)	59 (43–85)	63.5 (45–79)	63 (43–85)
Age ≥ 60 years, n (%)	6 (40)	17 (77)	23 (62)
Male, n (%)	9 (60)	13 (59)	22 (59)
Median IgM, g/dL at baseline (range)	3.49 (1.18–6.63)	3.00 (0.81–8.64)	3.11 (0.81–8.64)
Median Hgb, g/dL (range) at baseline	9.8 (5.3–12.0)	9.6 (7.0–13.2)	9.8 (5.3–13.2)

*Hgb, hemoglobin; Total, TGA+TGB

Results

Prior therapy (n=37 subjects)

Table 2. Prior Therapy			
	TGA n=15	TGB n=22	Total n=37
No prior therapy, n (%)	3 (20)	6 (27)	9 (24)
Previously treated, n (%)	12 (80)	16 (73)	28 (76)
Median number of therapies* (range)	3 (2–5)	2.5 (1–4)	3 (1–5)
Prior rituximab, n (%)	11 (73)	14 (64)	25 (68)
Prior purine analog, n (%)	7 (47)	7 (32)	14 (38)

*Does not include untreated patients

Total response rates (PR+MR) by disease characteristics

Table 3. Total Response Rate (PR+MR ^a) by Disease Characteristics			
	TGA n=15	TGB n=22	Total n=37
All patients, % (n/N)	47 (7/15)	68 (15/22)	59 (22/37)
Prior therapy, % (n/N)			
Yes	42 (5/12)	69 (11/16)	57 (16/28)
No	67 (2/3)	67 (4/6)	67 (6/9)
P value	0.569	1	0.711
Prior rituximab, % (n/N)			
Yes	36 (4/11)	64 (9/14)	52 (13/25)
No	75 (3/4)	75 (6/8)	75 (9/12)
P value	0.282	1	0.286
Baseline IgM level, % (n/N)			
< 4 g/dL	67 (6/9)	63 (10/16)	64 (16/25)
≥ 4 g/dL	17 (1/6)	83 (5/6)	50 (6/12)
P value	0.119	0.616	0.488

^aNo Crs described

Improvement in Anemia

- 15 of 26 (58%) patients with baseline hemoglobin (Hgb) <11 g/dL had a Hgb increase >3 g/dL

Table 6. Improvement in Hemoglobin			
	TGA	TGB	Total
Subjects, n	15	22	37
Baseline Hgb < 11.0 g/dL, n	12	14	26
Subjects with > 3.0 g/dL increase in Hgb, n (%)	6 (50)	9 (64)	15 (58)

*Total, TGA+TGB

Conclusions

- In the study ofatumumab is clinically active in patients with WM with an acceptable toxicity profile and a low incidence of IgM flare
- ORR to ofatumumab was 59% (TGA 47%, TGB 68%)
 - 50% ORR (TGA 17%, TGB 83%) in patients with IgM ≥ 4.0 g/dL
 - TGB patients achieved ORR >60% in all patient groups regardless of prior therapy or baseline IgM level
 - Higher dose of ofatumumab (2000 mg) seemed to be more effective in
 - patients previously exposed to rituximab or
 - patients with high tumor burden (IgM ≥ 4.0 g/dL)
 - RC improved response in 4 of 12 patients

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A phase I/II, dose-escalation study of daratumumab, a CD38 mAb in patients with multiple myeloma – Preliminary safety data

ASH abstract #1873

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Introduction

- Multiple myeloma (MM) accounts for approximately 1% of all malignancies and 10% of all hematological malignancies.
- Proliferating MM cells displace the normal bone marrow leading to dysfunction in normal hematopoietic tissue and destruction of the normal bone marrow architecture.
- Currently, no cure is available for patients with this malignant disease.
- Relapsed or refractory patients who are not eligible for autologous stem cell transplantation have a poor prognosis.

Introduction (cont.)

- MM cells exhibit very strong expression of CD38 transmembrane glycoprotein molecules.
- Daratumumab is a human CD38 monoclonal antibody with broad spectrum killing activity.
- Daratumumab has been shown to inhibit growth of CD38-expressing tumor cells in SCID mouse xenografts.

Objectives

- Primary objective:
 - Establishment of the safety profile of daratumumab when given as monotherapy in patients with MM, relapsed or refractory to at least two different prior therapies.
- Secondary objective:
 - Establishment of maximal tolerated dose (MTD) for future studies with daratumumab.
 - Evaluation of efficacy of daratumumab when given as monotherapy in patients with MM.

Methods

- This first-in-human study consists of two parts:
 - Part 1 dose-escalation to define the MTD;
 - Part 2 cohort expansion of MTD or maximal dose from Part 1 using an extended dose-schedule for 24 weeks.

- Eligible criteria:
 - Patients are ≥ 18 years,
 - diagnosed with MM,
 - ineligible for ASCT,
 - requiring systemic therapy,
 - considered relapsed or refractory to at least two different prior therapies.

Methods (cont.)

- Patients receive 2 pre- and 7 full-dose infusions of daratumumab over a 9-weeks period.
- The study design encompasses an accelerated dose escalation: 3 + 3 patients per cohort with the possibility to limit exposure to 1 patient in the first 2 cohorts depending on safety data.
- The doses range from 0.005 mg/kg to 24 mg/kg.
- Premedication consisting of steroids, acetaminophen and antihistamine is administered before all infusions.

Baseline characteristics and demography

Characteristic	<=0.5 mg/kg (N=11)	1 mg/kg (N=6)	2 mg/kg (N=3)	4 mg/kg (N=3)	Total (N=23)
Gender, n					
Male/Female	7/4	3/3	3/0	1/2	14/9
Age, years					
Median (range)	62 (42-76)	63 (45-71)	64 (60-71)	64 (62-66)	64 (42-76)
Prior therapeutic regimens					
Median (range)	6 (2-9)	5.5 (3-8)	8 (6-10)	6 (3-6)	6 (2-10)
Years since MM diagnosis					
Median (range)	5.0 (1.8-12.3)	5.1 (2.7-9.1)	8.4 (6.6-8.9)	5.7 (4.7-12)	5.7 (1.8-12.3)
Body weight					
Median (range)	78 (60-90)	85 (67-117)	94 (92-108)	70 (68-71)	80 (60-117)
ECOG PS					
0	5	0	0	2	7
1	6	5	3	1	15
2	0	1	0	0	1

Comment: The patient population is heavily pretreated with a median of 6 prior lines of therapy.

Results

- Safety data for 23 patients, including dose range from 0.005 mg/kg up to 4 mg/kg cohort, were collected.
- Five SAEs were assessed as related to daratumumab.
 - One patient had anemia grade 3 & thrombocytopenia grade 4 (0.1 mg/kg), one patient had elevated liver enzyme (AST) grade 3 (1 mg/kg). Based on these 2 DLT events, 3 more patients were enrolled in the 0.1 mg/kg and 1.0 mg/kg cohorts.
 - One patient experienced a grade 3 bronchospasm (2 mg/kg) and one patient experienced cytokine release syndrome grade 2 (0.1 mg/kg). Both were non-DLTs.
- All patients recovered after relevant treatment. Since implementation of pre-medication before all infusions, steroids for 2 days following infusion and dilution of trial drug, no serious infusion related AEs have been reported.

Overall summary of related AEs

(Number of events)	≤ 0.5 mg/kg (N=11)	1 mg/kg (N=6)	2 mg/kg (N=3)	4 mg/kg (N=3)	Total (N=23)
Patients	11	6	3	3	23
Related non-serious grade 3 AEs	3	0	0	2	5
Related SAEs	3	1	1	0	5

Incidence of most frequent AEs reported

(% of patients)	≤0.5 mg/kg (N=11)	1 mg/kg (N=6)	2 mg/kg (N=3)	4 mg/kg (N=3)	Total (N=23)
Pyrexia	55	17	0	0	30
Cough	36	0	33	0	22
Free hemoglobin	45	0	0	0	22
Anemia	36	17	0	0	22
Dizziness	18	17	0	33	17
Hemolysis	18	33	0	0	17
Flu-like illness	0	33	33	0	13
Nausea	18	0	0	33	13
Lymphopenia	0	33	33	0	13
Monocytopenia	0	33	33	0	13

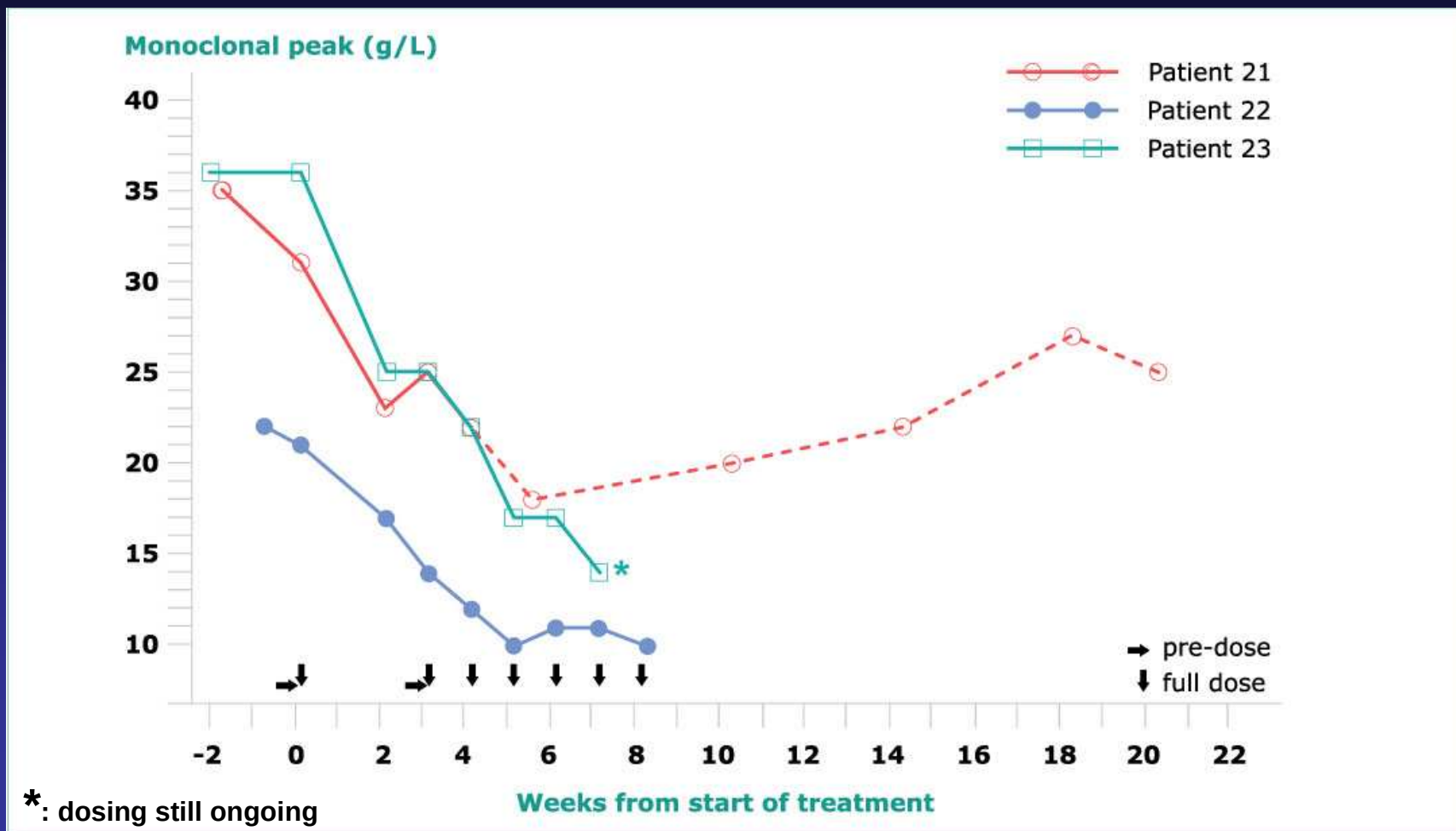
Incidence of most frequent AEs reported in >2 pts.

Maximum reduction in M-component

Cohort	n/N	Max reduction in M-component in patients with reduction	
		Serum	Urine
≤ 1 mg/kg	3/17	12 % 14 % 19 %	22 % ^ ^
2 mg/kg	1/3	^	55 %
4 mg/kg	3/3	49 % 55 % 61 %*	^ 73 % *^

*: dosing still ongoing; ^: not measurable at baseline

M-component reduction in 4 mg/kg cohort



Conclusions

- In the study daratumumab shows a favorable safety profile as monotherapy in patients with MM in doses up to and including 4 mg/kg.
- The MTD has not been established yet.
- Based on the observed safety profile, further dose-escalation is ongoing.
- In the 4 mg/kg dose cohort, a 49-61% reduction in serum M-component was observed.

Next steps and Q&A

Jan van de Winkel, Ph.D.
President and CEO

In Summary

- Significant pipeline progress in 2011
 - Encouraging clinical data for ofatumumab & daratumumab
 - New pre-clinical data for HuMax-TF-ADC
- Next generation technologies moving forward
 - DuoBody large scale manufacturing validation
 - DuoBody-ADC concept introduced

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2012 Objectives

Managing Our Priorities

Priority	Milestone	Current Progress
Maximize value of ofatumumab	• Report Ph II/III F&A CLL refract. data • Ph III CLL mainten. safety interim data • Ph III DLBCL O vs R futility analysis • Report data multiple ISS studies	
Expansion Arzerra	• Launch & reimbursement new countries • Filing in new territory	
Daratumumab	• Report efficacy data Ph I/II MM study • Initiate Ph I/II combination studies • Complete partnering	
Expand pipeline	• Report proof-of-concepts ADC and DuoBody product candidates	
DuoBody platform	• Enter new collaboration • Advance platform	
Partnered programs	• Report progress pre-clinical programs • Report progress clinical programs • Enter new collaboration	
Manage and control cash burn	• Reduce cash burn & lengthen cash runway • Execute sale manufacturing facility	

Better Antibodies By Design

- Core competence, unique & in-depth antibody expertise
- Therapeutic antibodies at the heart of cancer treatment
- Broad pipeline of innovative technologies and products
- Genmab's range of antibody technologies at cutting edge of antibody field
- Working towards translating our technologies into products of the future
- Driving sustainable value and growth



Better Antibodies By Design

