Workshop

Efgartigimod Phase 2 Clinical Trial in ITP: Full Data

Cusatuzumab Phase 1/2 Clinical Trial in AML: Proof-of-Biology Data

3 December 2018, San Diego

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Agenda

12:00 – 12:35 PM

Proof-of-Concept of Efgartigimod (ARGX-113) in Immune Thrombocytopenia (ITP)

- Full data from Phase 2 clinical trial
- Nicolas Leupin, CMO, argenx
- Guest speaker: Prof. Dr. Adrian Newland, Barts London & Royal London Hospital

12:35 – 1:15 PM

Advancing Cusatuzumab (ARGX-110) in Acute Myeloid Leukemia (AML)

- Proof-of-biology data from Phase 1 dose escalation trial
- Hans de Haard, CSO, argenx
- Guest speaker: Prof. Dr. Adrian Ochsenbein, Bern Cancer Center, Inselspital, University of Bern

1:15 – 1:30 PM

Q&A

Guest Speakers

Prof. Dr. Adrian Newland

- Professor of Haematology at Barts and the London NHS Trust
- Expert in haematological malignancy and particular interest in immunohaematology, studying the molecular basis of the autoimmune disease, in particular thrombocytopenia, and piloting the clinical use of novel treatments
- Developed the Leukaemia and Bone Marrow transplant unit in the early 1980s
- Centre Lead for Haematology in the Medical School, Director of Pathology for the Trust and is Clinical Director of the North East Thames Cancer Network

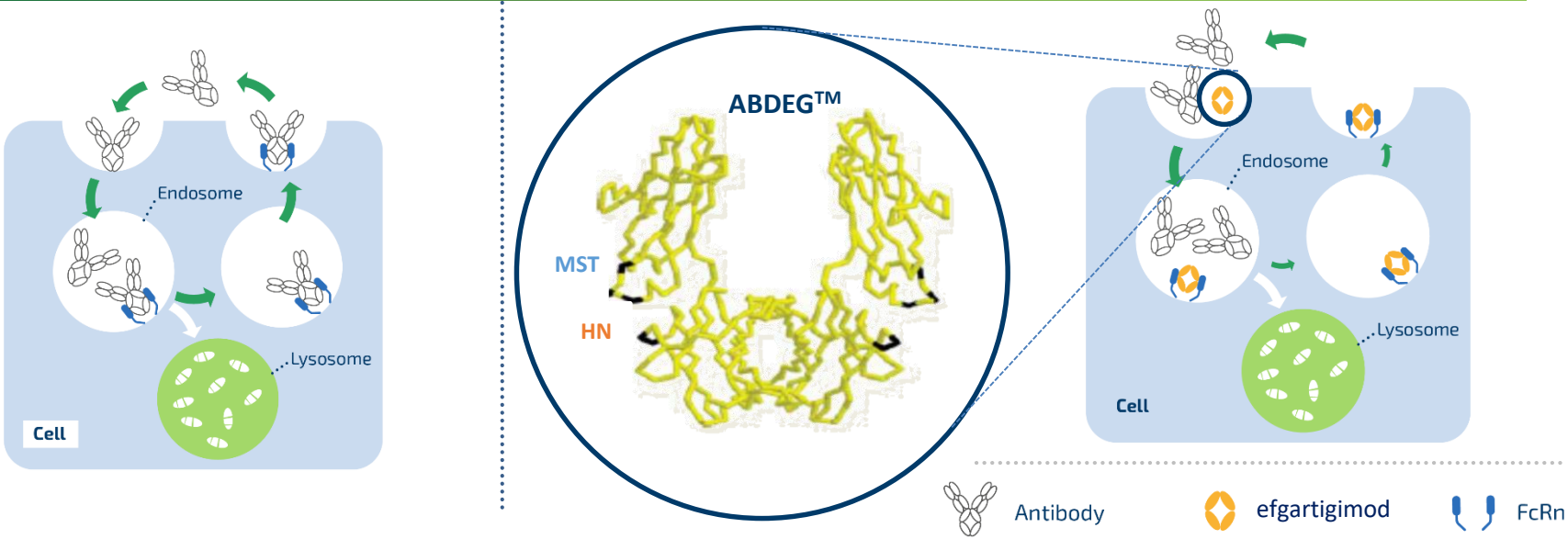
Prof. Dr. Adrian Ochsenbein

- Professor of Bern Cancer Center, Inselspital, University of Bern
- Expert in cancer/leukemia stem cells which are the origin of the disease and responsible for relapse after successful chemotherapy in AML ao. Studies generate broad understanding of translational research from animal studies to clinical applications
- Member of the National Research Council
- Awarded the Otto Naegeli Prize 2016 in recognition of the excellent scientific work as a clinically active medical oncologist

Efgartigimod:
A Pipeline-in-a-Product Opportunity

Efgartigimod: Human IgG1 Fc Fragment with ABDEG™ Mutations Exploits Natural Fc/FcRn Interaction

IgG antibodies recycle through FcRn(1)… **efgartigimod potently blocks FcRn…** **leading to IgG elimination(2)**



- Natural ligand binding: complex of efgartigimod and FcRn resides mainly in endosomal recycling compartment avoiding lysosomal degradation
- Improves affinity to FcRn in pH dependent manner thereby providing relatively long half-life of Fc fragment and excellent biodistribution
- Cannot engage FcγReceptors and does not recruit effector cells (3)(4)

(1) Roopenian et al. 2007, Nat Rev Immunol.
(2) Vaccaro et al. 2005, Nat Biotech.
(3) Ulrichts et al. 2018, J Clin Invest.
(4) argenx data

Primary Adult Immune Thrombocytopenia (ITP) – a Severe Autoimmune Disorder

What is ITP?

- Rare autoimmune bleeding disease
  - Estimated 69,300[1] patients in US
  - ~80% diagnosed with primary ITP
    - Newly diagnosed: ~3,000 – 7,500 patients [1]
    - Persistent: ~4,500 patients[2]
    - Chronic: ~43,000 patients[2]
- Symptoms include: mild bruising to severe bleeding, fatigue, fear of bleeding, impact on work and social activities, depression
- Relevance of platelet counts
  - ≤ 30 X 10^9/L generally accepted trigger for therapy
  - Improvement to ≥ 50 X 10^9/L considered clinically meaningful

Limited treatment options

- Multiple iterations on corticosteroids & IVIg
- TPO-receptor agonists*
- Splenectomy
- Immunomodulatory agents

** Generated global revenues of $1.5 billion in 2017*[3][4]

Unmet need in ITP

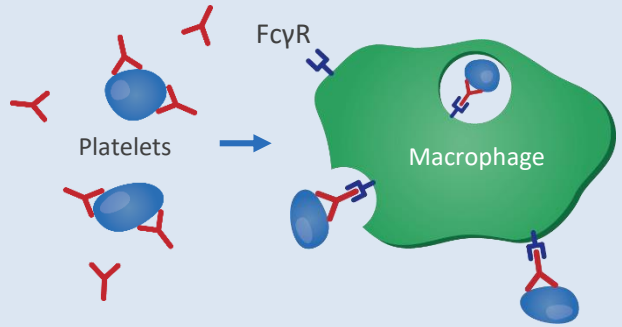
- Current treatments – limited efficacy and significant side effects
- No real treatment paradigm exists – trial & error
- Patients adapt lifestyle to cope with disease burden and treatment side effects

(1) Fogarty et al. 2004 Hematol Oncol Clin North Am., Feudjo-Tepie et al. 2008. J Thromb Haemost., Segal et al. 2004, Am J Hematol.
(2) Extrapolated from Moulis et al. 2017, Am J Hematol.
(3) Novartis FY 2017
(4) Amgen FY 2017

Efgartigimod Targets All Pathogenic AutoAb Actions Simultaneously

Potential to eliminate cycling between therapies based on trial-and-error

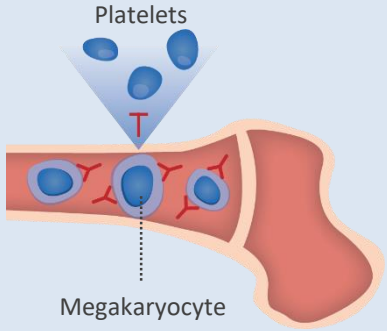
1. Accelerate platelet clearance



IVIg Tavalisse Splenectomy

efgartigimod

2. Inhibit platelet production

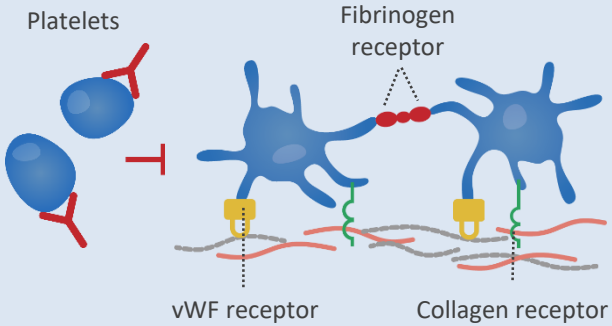


TPO-RA

efgartigimod

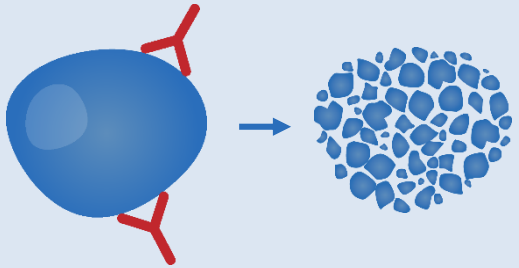
Autoantibodies

4. Interfere with platelet function



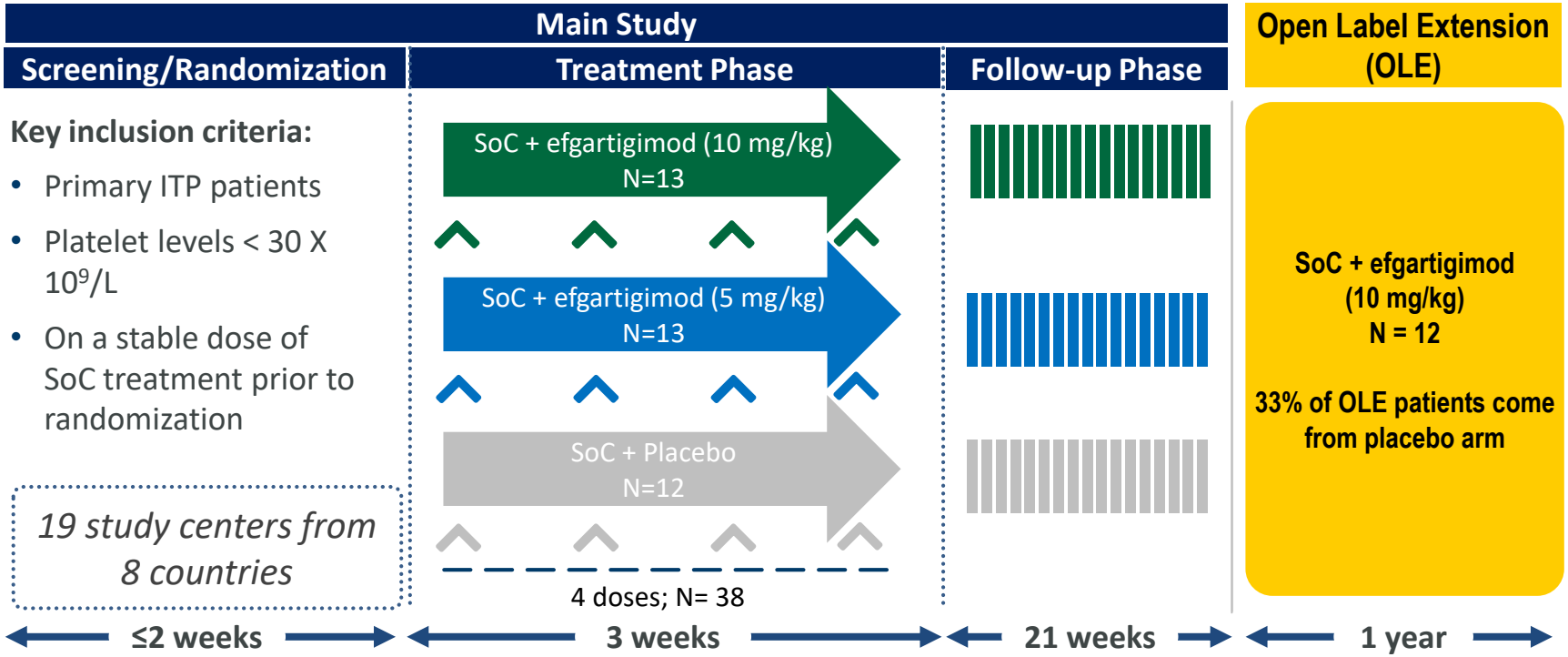
efgartigimod

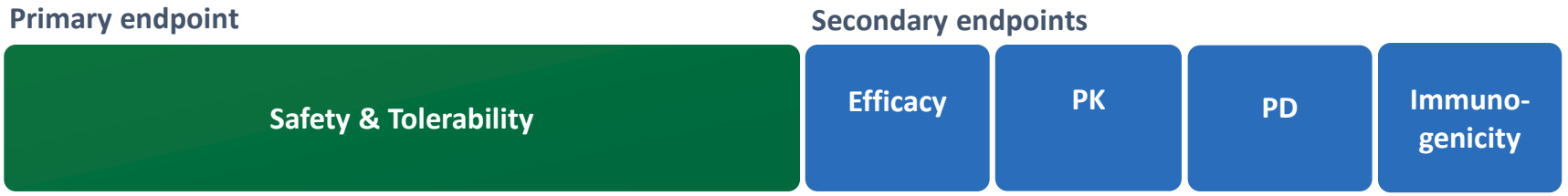
3. Induce platelet killing



efgartigimod

ITP Amended Phase 2 Proof-of-Concept Trial Design





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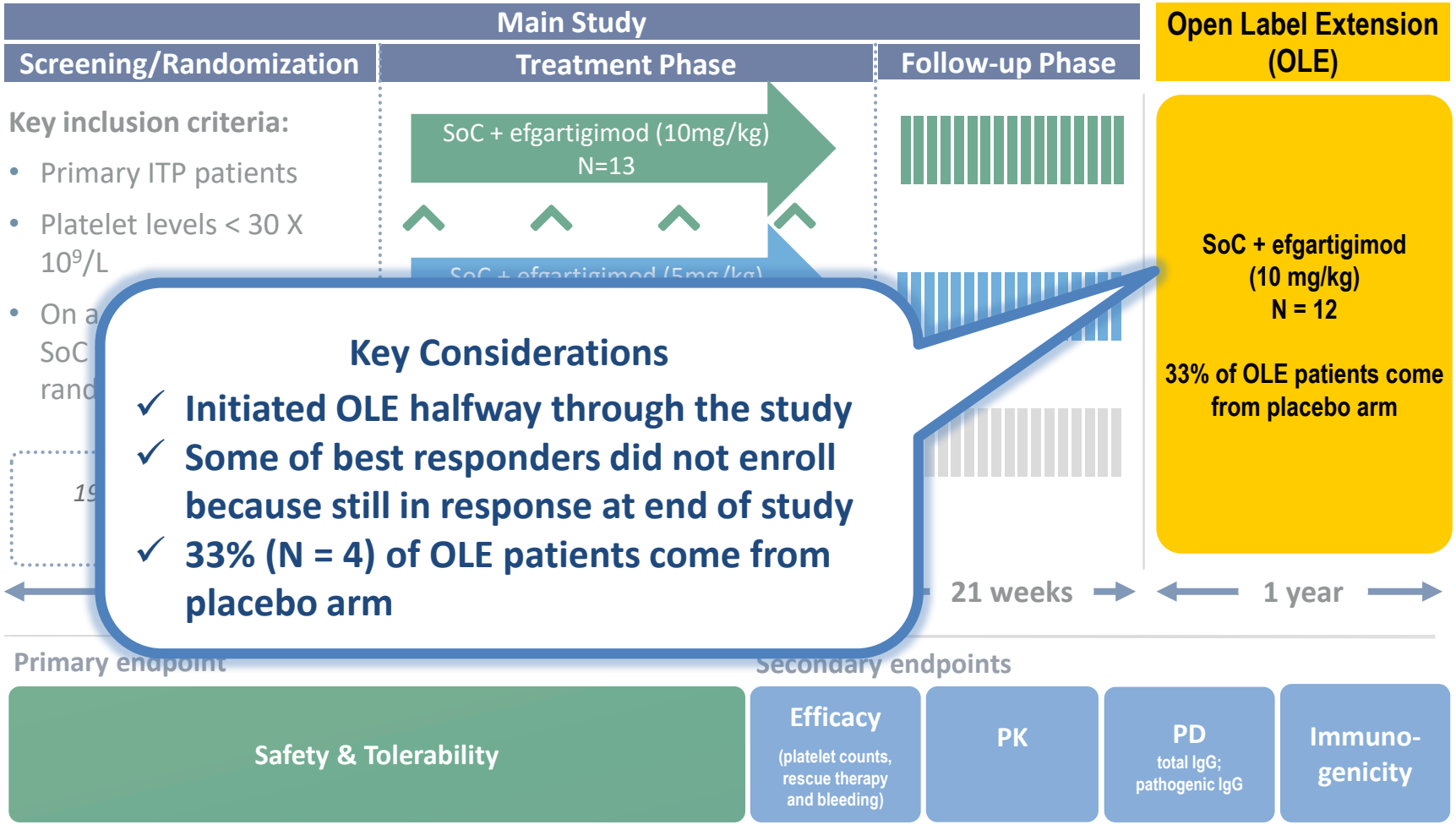


ITP Phase 2 Clinical Trial: Results

ITP Phase 2 Baseline Population and Disease Characteristics

	Placebo (n = 12)*	Efgartigimod: 5 mg/kg (n = 13)	Efgartigimod: 10 mg/kg (n = 13)**
Age, median (range)	38.5 (19 - 69)	41.0 (22 - 77)	46.0 (29 - 62)
Gender, n (%)			
• Male	5 (41.7)	4 (30.8)	9 (69.2)
• Female	7 (58.3)	9 (69.2)	4 (30.8)
Race, n (%)			
• White	11 (91.7)	12 (92.3)	13 (100)
• Not reported	1 (8.3)	1 (7.7)	-
ITP Classification, n (%)			
• Newly diagnosed (≤3 months)	-	2 (15.4)	-
• Persistent (>3 and <12 months)	3 (25.0)	1 (7.7)	4 (30.8)
• Chronic (≥12 months)	9 (75.0)	10 (76.9)	9 (69.2)
Duration of ITP, median years (range)	3.5 (0.3 - 47.8)	4.5 (0.1 - 34.2)	5.4 (0.7 - 28.7)
Baseline platelet count, mean, k/µL (			15 (5 - 35)
Baseline platelet count of <15k/µL, N			7 (53.8)
SoC a			
• C		10 (76.9)	6 (46.2)
• T		4 (30.8)	3 (23.1)
• I		-	1 (7.7)
• W		2 (15.4)	5 (38.5)
• Other n (%)	1 (8.3)	1 (7.7)	-

Very refractory population

50% of patients with baseline platelet counts below 15k/µL

- Four placebo patients were discontinued before the end of the main study ** Two 10mg/kg patients were discontinued before receiving all 4 infusions argenx data

Favorable Tolerability Profile Consistent with Previous Studies

Treatment-emergent adverse events balanced between active and placebo arms

- **Tolerability profile consistent with Phase 2 myasthenia gravis (MG) and Phase 1 healthy volunteer (HV) trials**
- **TEAEs mostly mild in severity (grade 1)**
- **No deaths or TEAEs leading to discontinuation of treatment reported***

Bleeding TEAEs not included

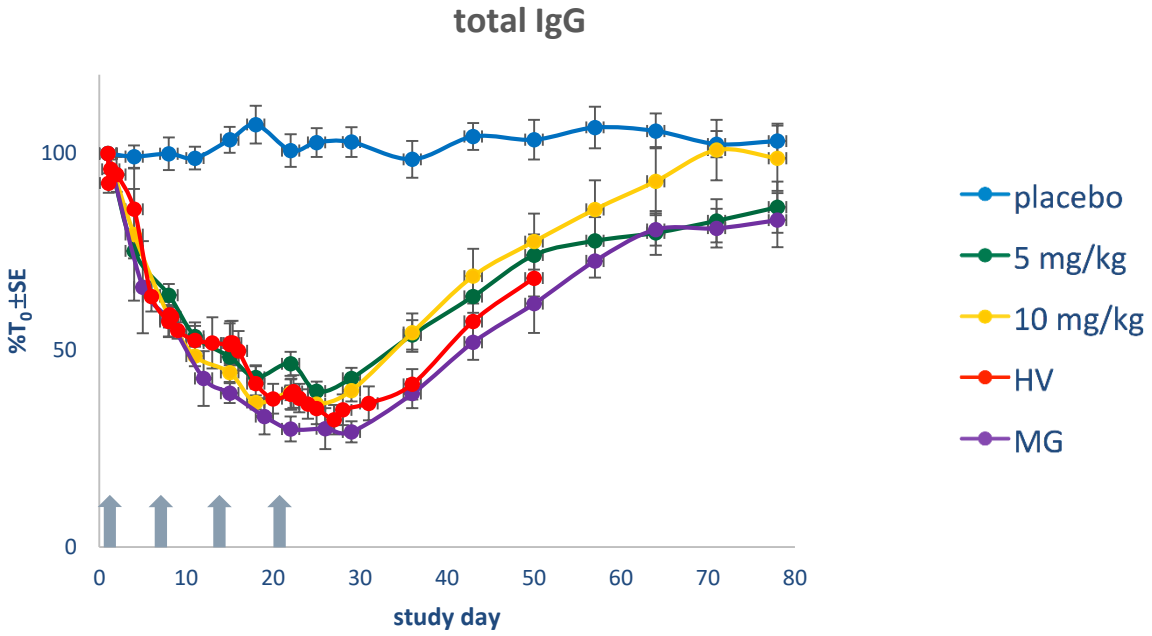
Treatment Emergent Adverse Events (TEAEs) Reported in ≥ 2 subjects	Placebo (N = 12)	Efgartigimod 5 mg/kg (N = 13)	Efgartigimod 10 mg/kg (N = 13)
Most common TEAEs N (%)			
• Headache	2 (16.7)	1 (7.7)	-
• Hypertension	1 (8.3)	-	2 (15.4)
• Vomiting	-	-	2 (15.4)
• Cystitis	-	1 (7.7)	1 (7.7)
• Rash	-	1 (7.7)	1 (7.7)
• Productive cough	1 (8.3)	1 (7.7)	-
TEAEs *deemed related* to study intervention N (%)			
• Headache	1 (8.3)	-	-
• Vomiting	-	-	1 (7.7)
• Pubic pain	1 (8.3)	-	-
• Vaginal discharge	1 (8.3)	-	-
• Amenorrhoea	1 (8.3)	-	-

* One thrombocytopenia downgraded per protocol after database lock

argenx data: Table 14.3.1.2a & 14.3.1.5a - Treatment-Emergent Adverse Events by System Organ Class, Preferred Term and Relationship to Study Drug - Main Study

Efgartigimod Leads to Lasting IgG Reduction Across Studies

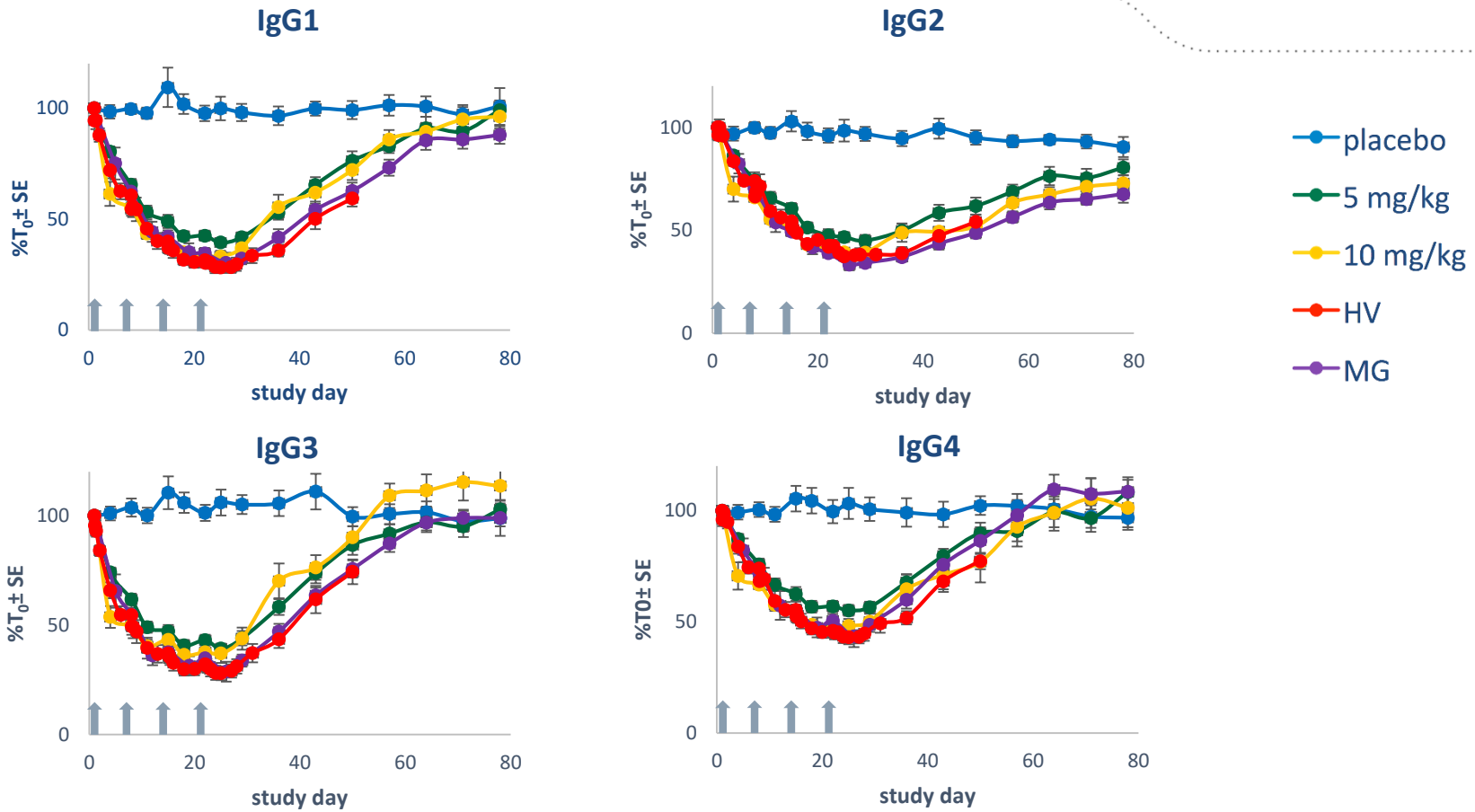
Total IgG levels in efgartigimod studies to date (Healthy Volunteers, MG, ITP)



- Pharmacodynamics (PD) closely align with Phase 1 trial in HV and Phase 2 trial in MG
- IgM, IgA and albumin levels not affected (data not shown)
- Half-life: approx. 5 days
- Pharmacokinetics (PK) very similar to Phase 1 trial in HV and Phase 2 trial in MG (data not shown)
- Low titer of anti-drug antibodies (ADA) seen in 16.7% placebo patients vs. 30.8% efgartigimod patients (10 mg/kg) with no apparent effect on PK/PD

Lasting IgG Reductions Across IgG Subtypes

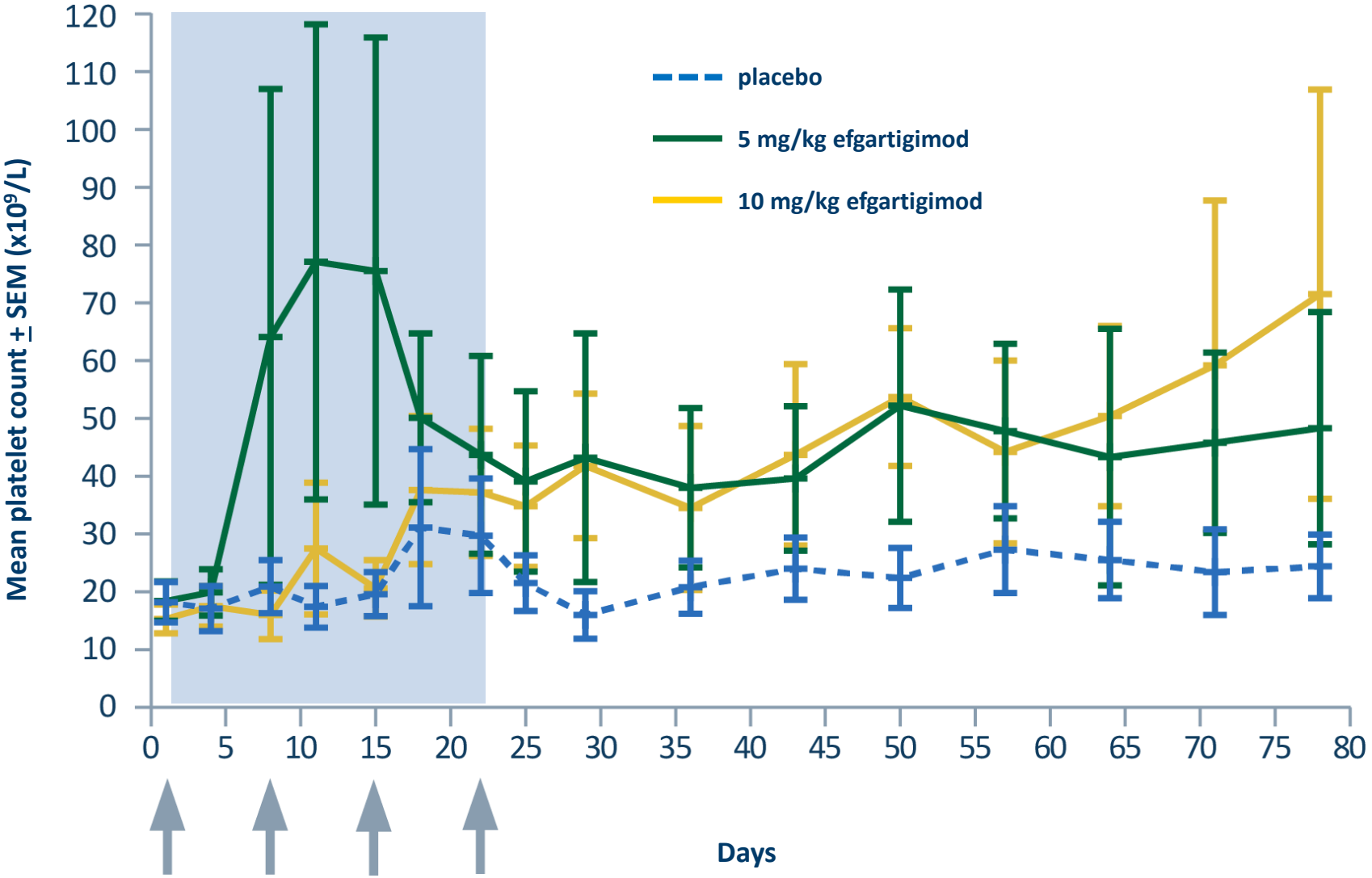
Similar reduction levels achieved across studies



- IgG subtypes reduced in all patients in active arms (auto-antibodies in ITP are IgG1/3)
- Relatively small differences observed between 5 and 10 mg/kg cohort
- Similar reduction levels achieved with 10 mg/kg dose compared to previous studies
- All patients tested positive for platelet associated auto-antibodies (GP IIb/IIIa; GP Ib/IX; GP Ia/IIa)
- Platelet associated auto-antibody signal reduced by maximally 53-97% in 8/12 efgartigimod responders

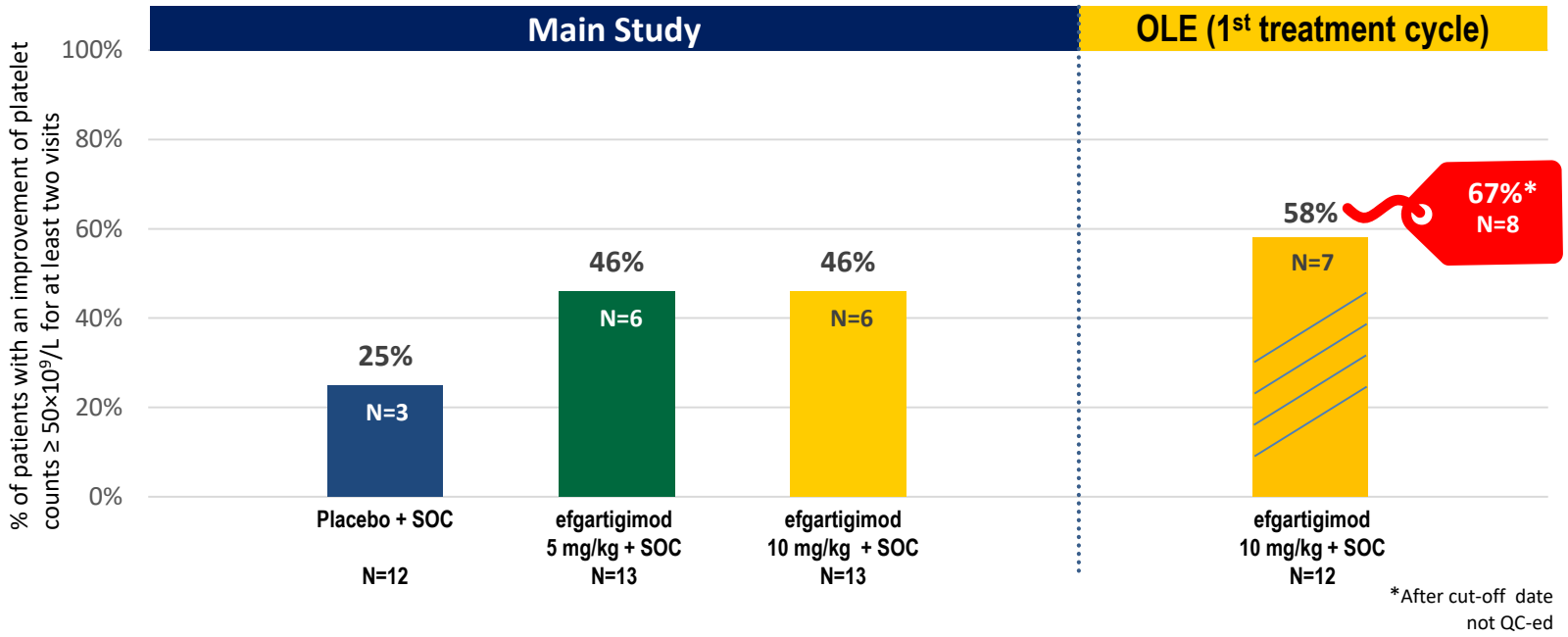
Clinically Meaningful Improvements in Platelet Counts in Active Arms

Separation from placebo starts at maximum PD and lasts through study follow-up



Strong Improvement of Platelet Counts Across Doses

46-67% of patients exceeded platelet counts ≥ 50X10^9/L during at least two visits

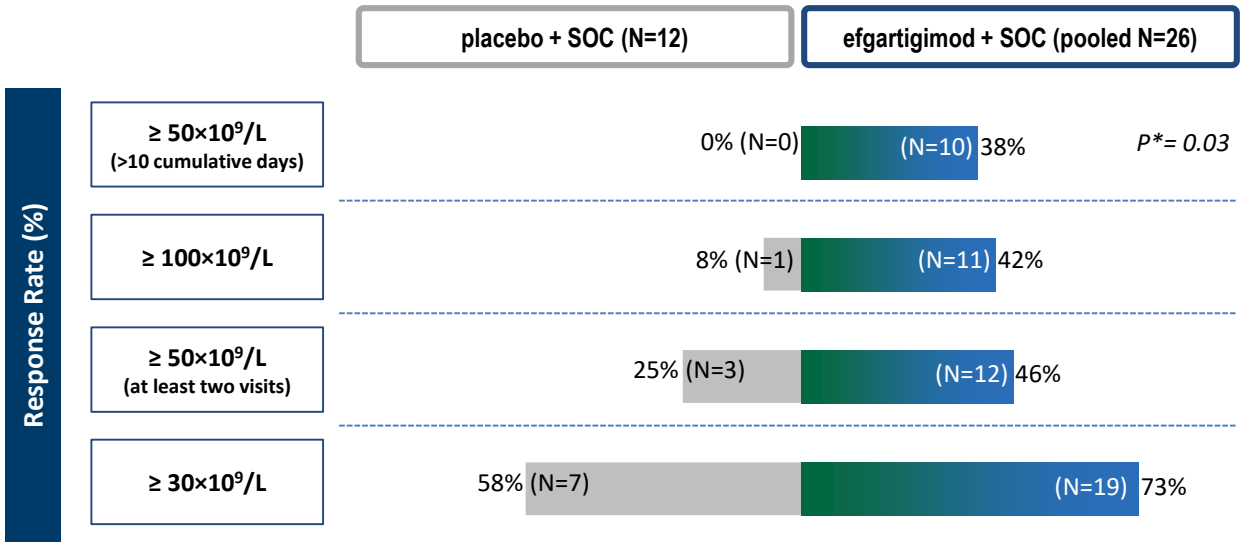


- OLE acts as true fourth cohort since patients' platelets had to fall below 30x10^9/L to be eligible for a treatment cycle; patients still in response from primary study were not eligible
- Responses seen across newly diagnosed (in 5mg/kg arm), persistent and chronic ITP patients

Robust Improvement of Platelet Count with Durability

Increasing differentiation from placebo for increasing efficacy hurdle

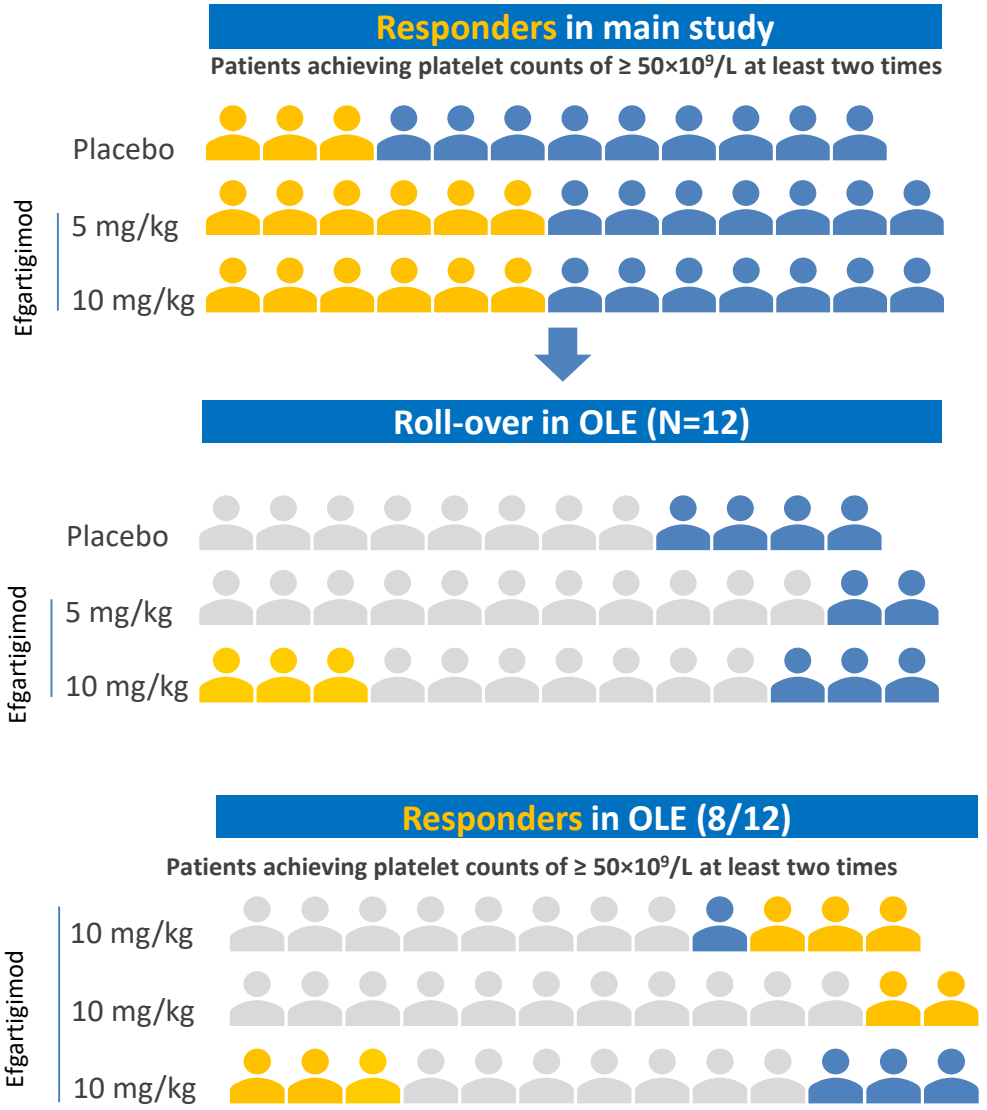
Post-hoc analysis of increasing thresholds of efficacy



- Efgartigimod generated therapeutic activity at multiple relevant thresholds of efficacy
- Duration of platelets remaining ≥50x10^9/L ranged from 1 - 20 weeks, with five patients above that platelet threshold for more than a month
- ≤ 30 X 10^9/L generally accepted trigger for therapy with improvement to ≥ 50 X 10^9/L considered clinically meaningful

Note: Increasing threshold analysis based exact logistic regression model with the baseline result as a factor

Responses in First Cycle of Open Label Extension



Responder

Non-responder main study and OLE

Patients not rolled over

Open Label Extension study

1st Cycle Analysis:

8 patients responded on efgartigimod (10 mg/kg):

- 3 Non-responders from placebo started to respond
- 2 Non-responders from 5 mg/kg treatment arm started to respond
- 3 Responders from 10 mg/kg treatment arm continued to respond

Validated Bleeding Assessment Measures

Bleeding events are hallmark of ITP and were not an exclusion criterion to study entry

Bleeding events

Adverse events

- **Mild**: Transient or mild discomfort & no medical intervention required
- **Moderate**: Mild to moderate limitation in activity & no or minimal medical intervention required
- **Severe**: Marked limitation in activity, some assistance usually required & medical intervention required, hospitalization possible
- **Life-threatening**

Bleeding assessment tools

WHO scale

General bleeding assessment widely used in clinical development

- **Grade 0**: No bleeding
- **Grade 1**: Petechial bleed
- **Grade 2**: Mild blood loss (clinically significant)
- **Grade 3**: Gross blood loss requires transfusion (severe)
- **Grade 4**: Debilitating blood loss, retinal/cerebral bleed (associated with fatality)

ITP-BAT scale

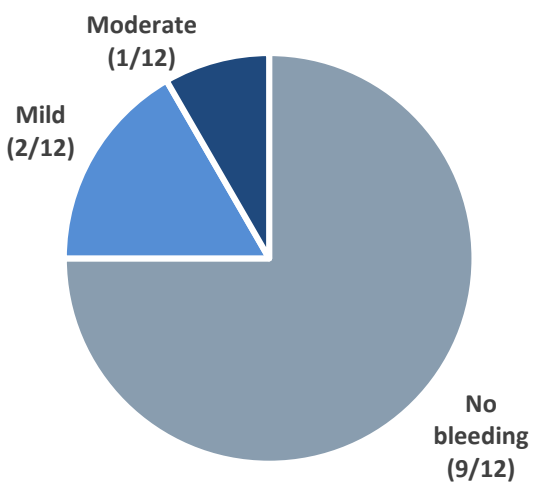
Consistent description of the bleeding phenotype in ITP in 3 domains: Skin, Mucosa and Organ grade (SMOG)

- **Grade 0:** No bleeding
- **Grade 1**: Reported without medical documentation
- **Grade 2 → 4:** Increasing severity, number and surface area
- **Grade 5**: Fatal bleeding

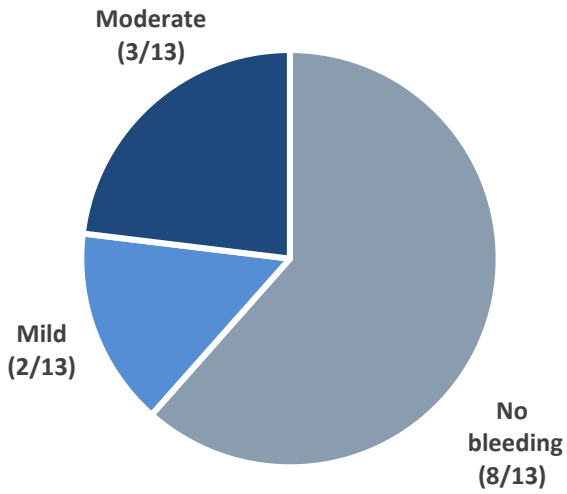
No Adverse Event Reports of Severe Bleeding

All bleeds in 10 mg/kg were mild

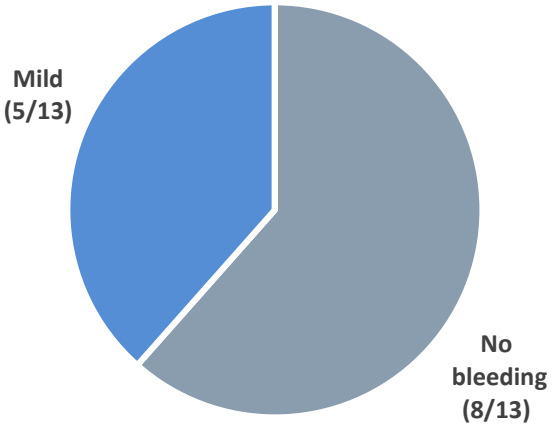
Placebo



5 mg/kg efgartigimod



10 mg/kg efgartigimod

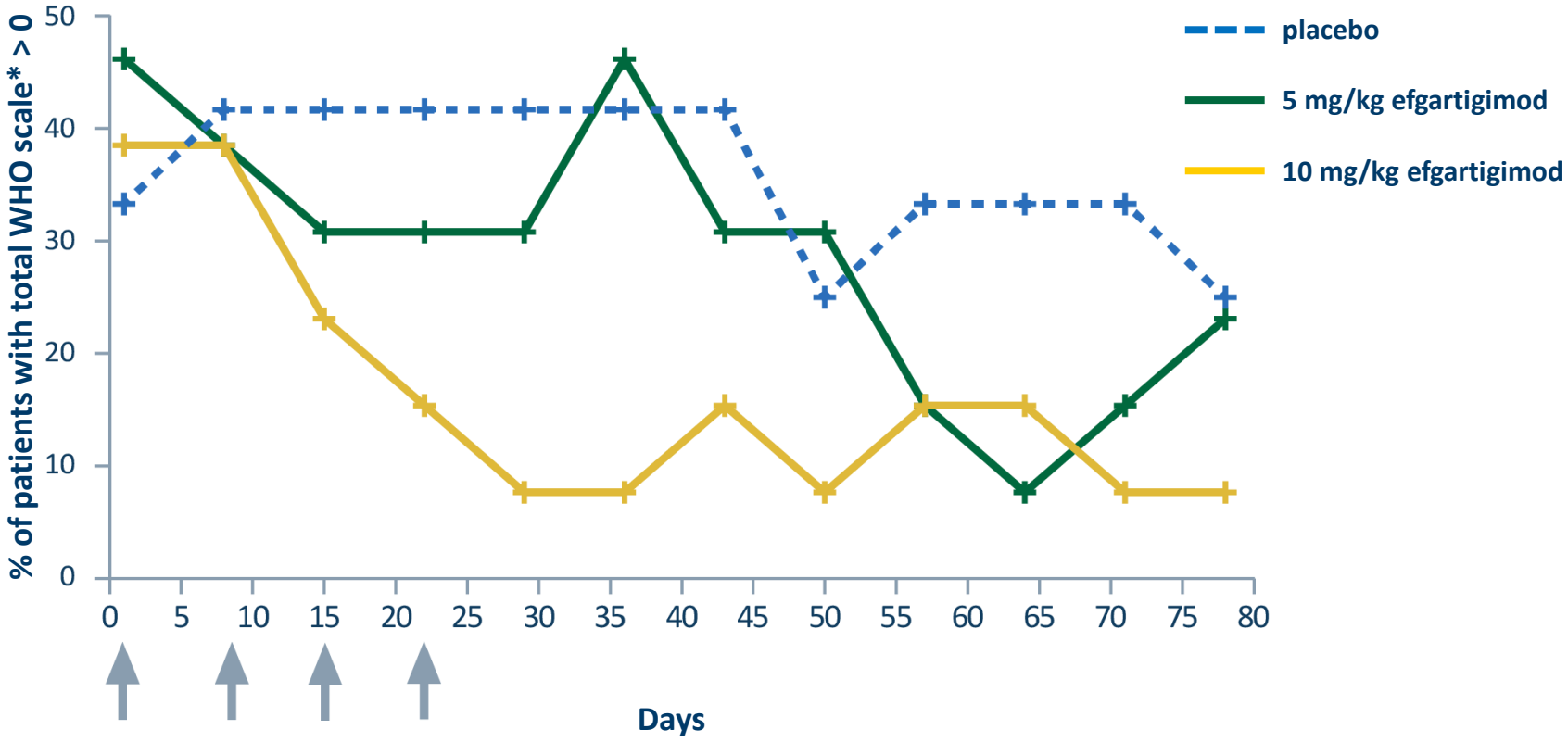


- Bleeding is hallmark of ITP disease; low platelet counts correlate with higher incidence of bleeding events
- No bleeding events deemed study drug related by investigator
- No severe bleedings in any patient
- No moderate bleeds occurred in 10 mg/kg arm; bleeds were all mild
- 5 patients in each treatment arm experienced at least one bleeding TEAE, compared to 3 in placebo cohort
- 35 bleeding events reported in 13/38 patients; 15 bleeds (37%) in 1 non-responder (data not shown)

Efgartigimod Reduces Incidence of Bleeding Compared to Placebo

Bleeding events in 10 mg/kg arm steadily decline and stay low following treatment

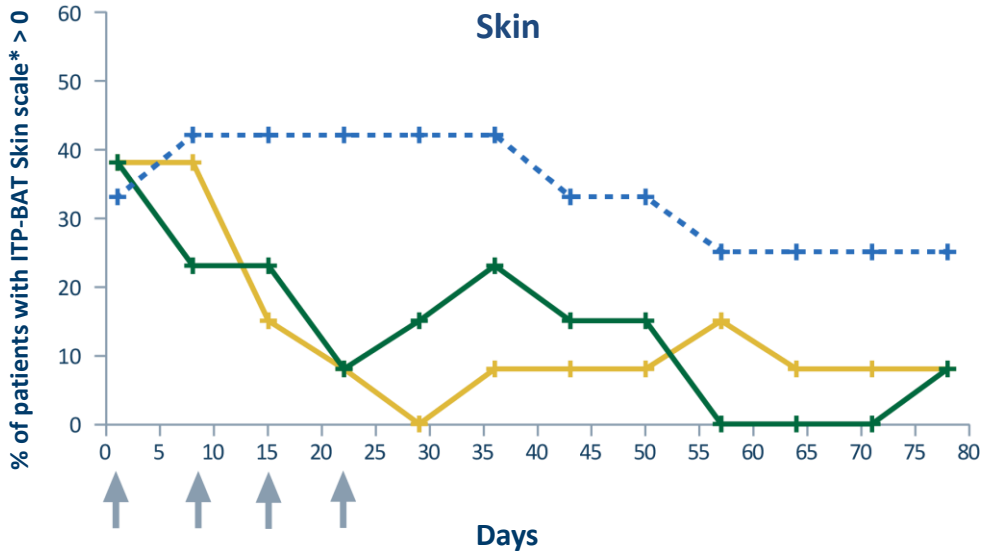
WHO scale in placebo versus 5 mg/kg and 10 mg/kg efgartigimod

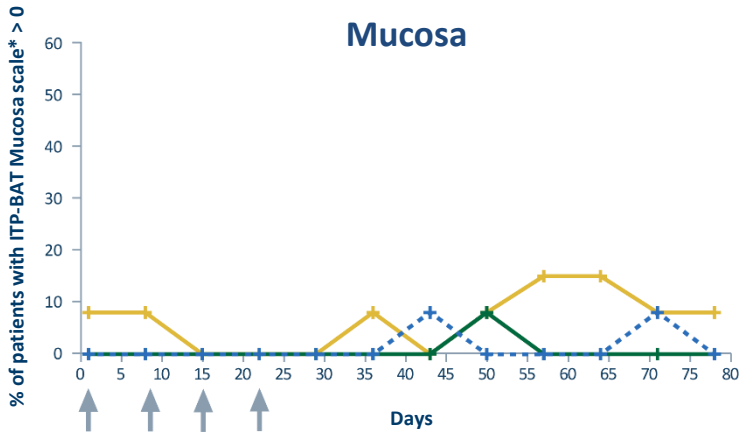


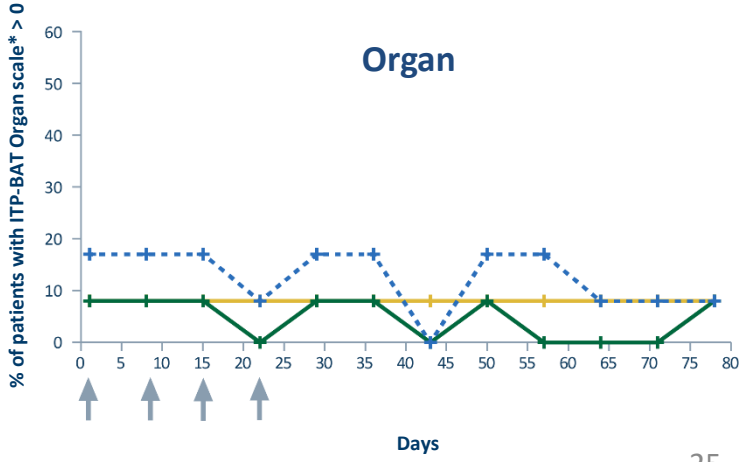
* Severity is graded from 0 to 4 – Only grade 1 and 2 were observed

Fewer Patients with Bleeds in Active Arms Versus Placebo Over Time

ITP-BAT/SMOG scale in placebo versus 5 mg/kg and 10 mg/kg efgartigimod





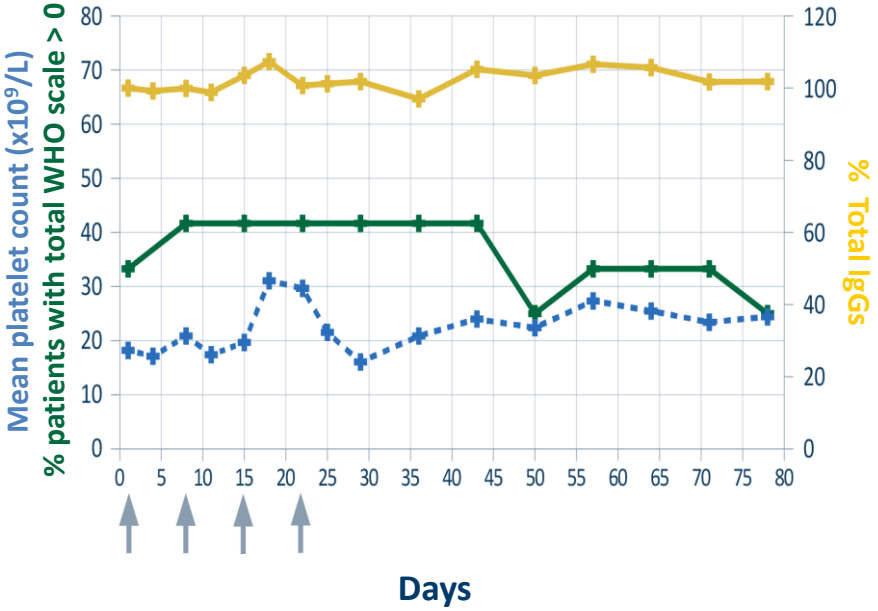


* Severity is graded from 0 to 5 – Only grade 1, 2 and 3 were observed

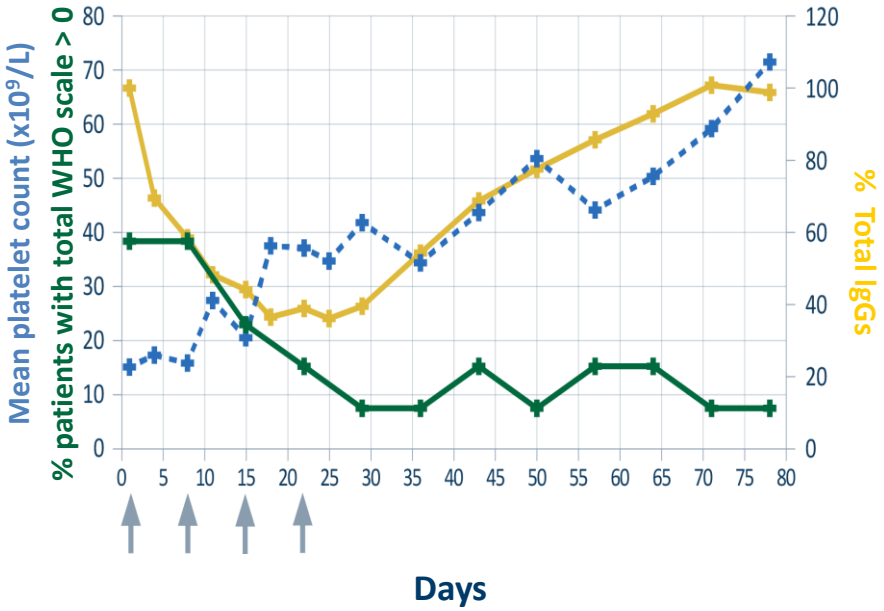
Reduction of Total IgGs Correlates with Increased Platelet Counts and Reduced Bleeding Events

Mean platelet counts versus total WHO scale versus total IgGs

Placebo



10 mg/kg efgartigimod



- % total IgGs
- Mean platelet counts (x10⁹/L)
- % patients with total WHO scale >0

ITP Phase 2 Results Establish Hematologic Beachhead

Novel approach beyond boosting platelet production or broad immuno-suppression

Favorable and consistent safety and tolerability profile

- No trends seen for infections or headaches across all studies
- No decreases in IgM, IgE, IgA or albumin

Robust efficacy signal in relapsed/refractory population after short drug exposure

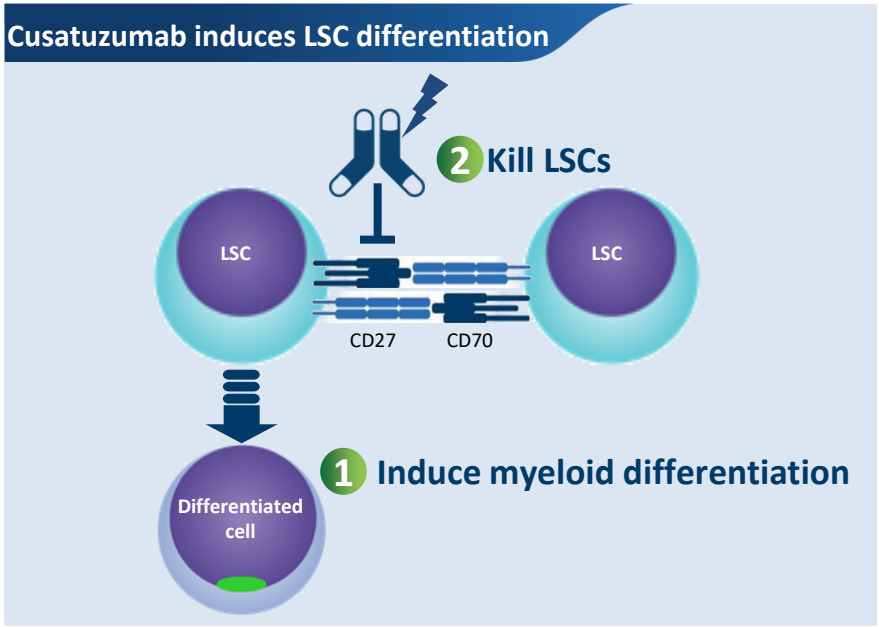
- Clinically meaningful increase in platelet counts over placebo
- 50% of patients came on study with platelets <$15x10^9$

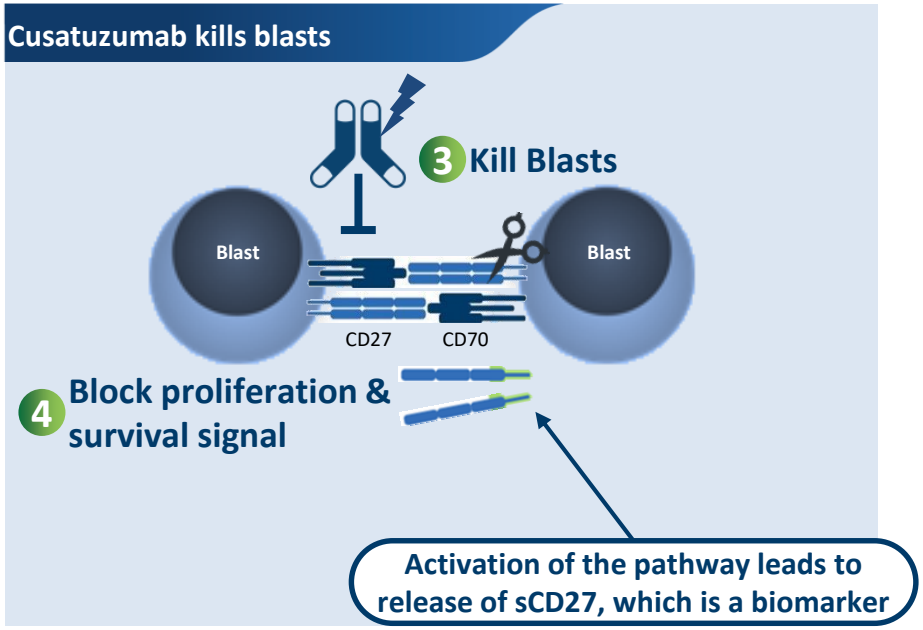
Strong correlation between IgG reduction, platelet count improvement and reduction of bleeding events

Data enable Phase 3 in ITP (IV) and launch of Phase 2 in ITP (SC)

Cusatuzumab: Selectively Targeting LSCs

Cusatuzumab: Unique MOA Targeting Acute Myeloid Leukemia (AML) Leukemic Stem Cells (LSCs) and Blasts





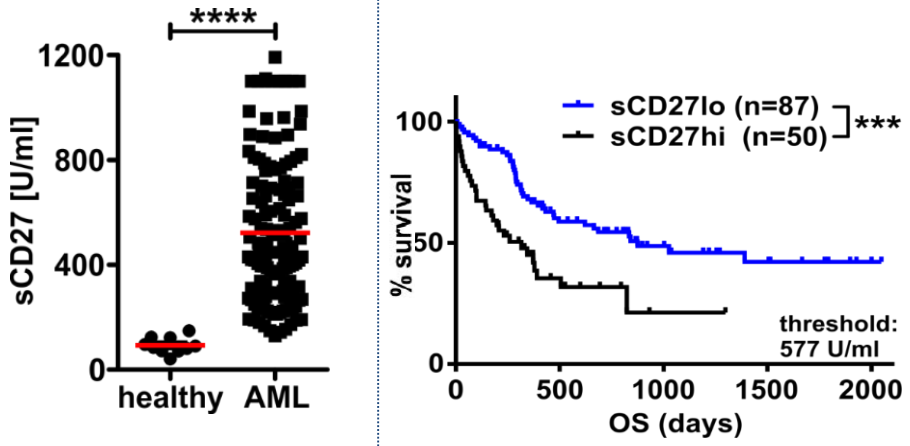
- First-in-class anti-CD70 ADCC enhanced SIMPLE Antibody™ which selectively targets LSCs and blasts in AML and other hematological indications
- CD70 expressed on ~86-100% of AML blasts; majority of malignant cells are CD70/CD27 double-positive

Silence et al. 2014, mAbs., Riether et al. 2017, J Exp Med.

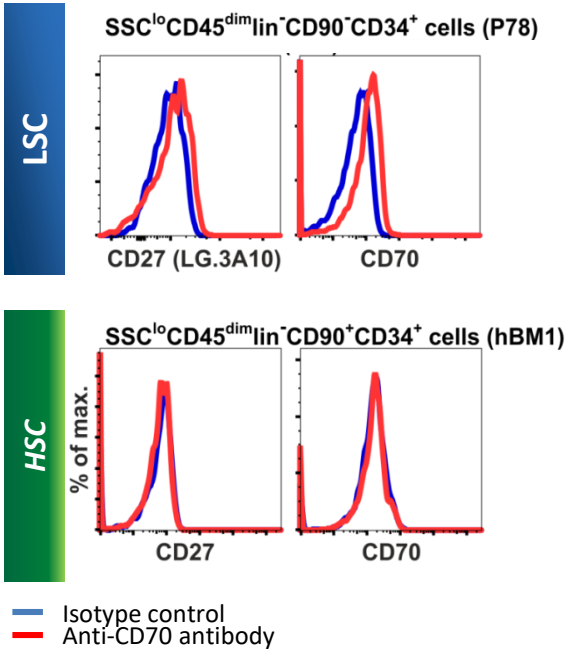
Selective Targeting of CD70 Expressed on Leukemic Stem Cells

Unifying rationale across risk and age classes in AML

Elevated sCD27 serum levels correlate with poor prognosis



CD70 is a selective LSC marker



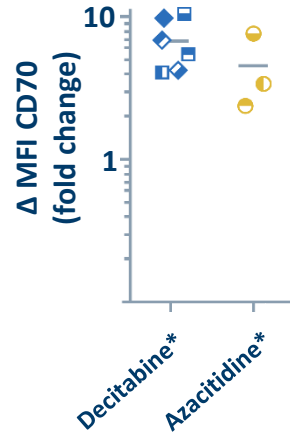
Legend: OS, overall survival.
Statistics: left: one-way ANOVA; middle: log-rank test. ***, P < 0.001.

- Elevated serum sCD27 in all newly diagnosed AML patients, regardless of risk category or age
- sCD27 levels are an independent negative prognostic marker in all newly diagnosed AML patients
- CD70 selectively overexpressed on LSCs, not on hematopoietic stem cells (HSCs)

Riether et al. 2017, J Exp Med.

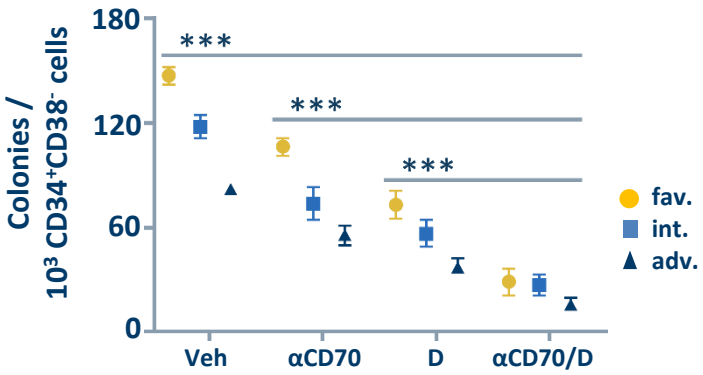
Cusatuzumab + Hypomethylating Agents Work Synergistically

HMA: Upregulated CD70

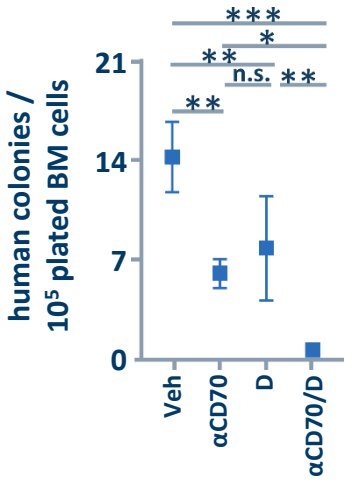


Combo: Reduced colony formation

Ex vivo colony formation assay



In vivo PDX model



Legend: αCD70: anti-CD70 Ab 41D12-D/cusatuzumab variant, adv.: adverse, BM: bone marrow, D: decitabine, fav. Favourable, int.: intermediate, LSC: FACS-purified leukemic stem/progenitor cells, *HMA SoC: D and A dosed 5 resp. 7 consecutive days, MFI: mean fluorescence intensity, PDX: patient-derived *in vivo* xenograft model in immunodeficient NSG mice, Veh: vehicle

- HMAs upregulate CD70 on AML leukemic stem cells – NOT on hematopoietic stem cells
- *Ex vivo*: HMA/cusa variant synergistically reduces colony formation
- *In vivo*: Transient treatment by HMA/cusa variant eradicates human LSCs in therapeutic model (not shown)

Hinterbrander ASH 2017: Blocking CD70/CD27 signaling in combination with hypomethylating agents eradicates human CD34⁺ AML stem and progenitor cells; manuscript in preparation

Ongoing Phase 1/2 Trial in Newly Diagnosed AML: Update Phase 1

Ongoing Phase 1/2 Combination Trial

Newly diagnosed AML patients unfit for intensive chemotherapy

Open label, non-controlled, non-randomized

Phase 1 – Dose Escalation

- **1 mg/kg** N = 3+3
- **3 mg/kg** N = 3+3
- **10 mg/kg** N = 3+3
- **20 mg/kg** N = 3+3

Endpoints

- Safety, tolerability
- Clinical outcome
- Translational data

Phase 2 – Proof of Concept at 10 mg/kg

Currently enrolling Phase 2

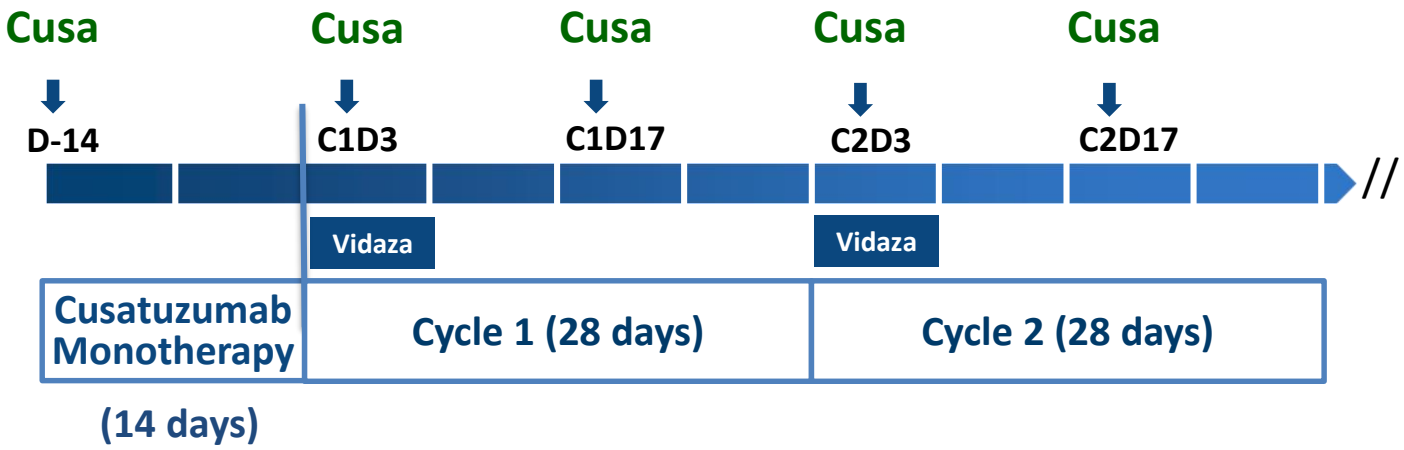
- Efficacy seen across doses in Phase 1 dose escalation
- Up to 21 patients to enroll in initial Phase 2 study with potential to expand enrollment to 40
- 10 mg/kg selected for Phase 2 to saturate bone marrow and maintain clean tolerability profile

Ongoing Phase 1/2 Combination Trial

Two weeks cusatuzumab monotherapy to assess impact on LSC biology

Cusatuzumab
1, 3, 10, 20 mg/kg
Biweekly IV

Vidaza
75 mg/m²
7d/month SC



Key inclusion criteria

- Newly diagnosed AML patients
- Unfit for intensive treatment or stem cell transplantation
- ≥20% blasts in the bone marrow by cytomorphology

Phase 1 Dose Escalation Population

Newly diagnosed patients with intermediate or adverse risk profiles

		1 mg/kg (N=3)	3 mg/kg (N=3)	10 mg/kg (N=3)	20 mg/kg (N=3)	Total (N=12)
Age (years)	Median	77	71	74	76	75
	Range	75-81	71-84	64-75	72-77	64-84
Gender	Male	2	1	2	2	7
	Female	1	2	1	1	5
AML Classification (WHO 2016)	NOS*	0	1	2	0	3
	With myelodysplasia-related changes	2	2	0	2	6
	Therapy related myeloid neoplasm	1	0	0	0	1
	Recurrent genetic abnormalities	0	0	1	1	2
Time since diagnosis (days)	Median	21	20	4	17	11.5
	Range	0-54	6-61	0-4	0-29	0-61
Risk categories#	Intermediate	1	2	2	1	6
	Adverse	2	1	1	2	6

* NOS: not otherwise specified; # ELN 2017

- Median age: 75 years
- Balanced distribution of intermediate or adverse risk profiles between different cohorts

argenx data

Vidaza Monotherapy Provides Limited Overall Response Rate

ORR in 30-35% range with significant side effects

Study	Patients (N)	ORR (%)	Adverse events (G3-G4)	%
Falantes *et al.* 2017	710	**35.5***	Pancytopenia Febrile neutropenia Infections	8 – 75 11 – 50 6 – 30
Dombret *et al.* 2015	231	**31.1****	Febrile neutropenia Neutropenia Thrombocytopenia Pneumonia Anemia Leukopenia Hypokalemia Infections	28 26 24 24 19 16 7 5

- 60% of newly diagnosed AML patients are more than 60 years old
- Hypomethylating agents (HMA) have no documented effect on leukemic stem cells responsible for relapse

* ORR defined as CR + CRi + PR
** ORR defined as CR + CRi + CRc-20 + PR
Dombret et al. 2015, Blood; Falantes et al. 2017, Leuk & Lymphoma.

Phase 1 Dose Escalation: No Obvious Toxicity on Top of Known Vidaza Toxicity

Cut-off: 15Oct18

Treatment Emerging Adverse Events (TEAEs)	Grade 3* events (N)	Grade 4 events (N)	Grade 5 events (N)
Anemia	16 (5)	1 (1)	
Thrombocytopenia	6 (4)	7 (4)	
Neutropenia	3 (2)	3 (3)	
Febrile Neutropenia	4 (4)		
Leukopenia		2 (2)	
Hypertension	2 (1)		
Multi-Organ Failure			1 (1)
Atrial Flutter		1 (1)	

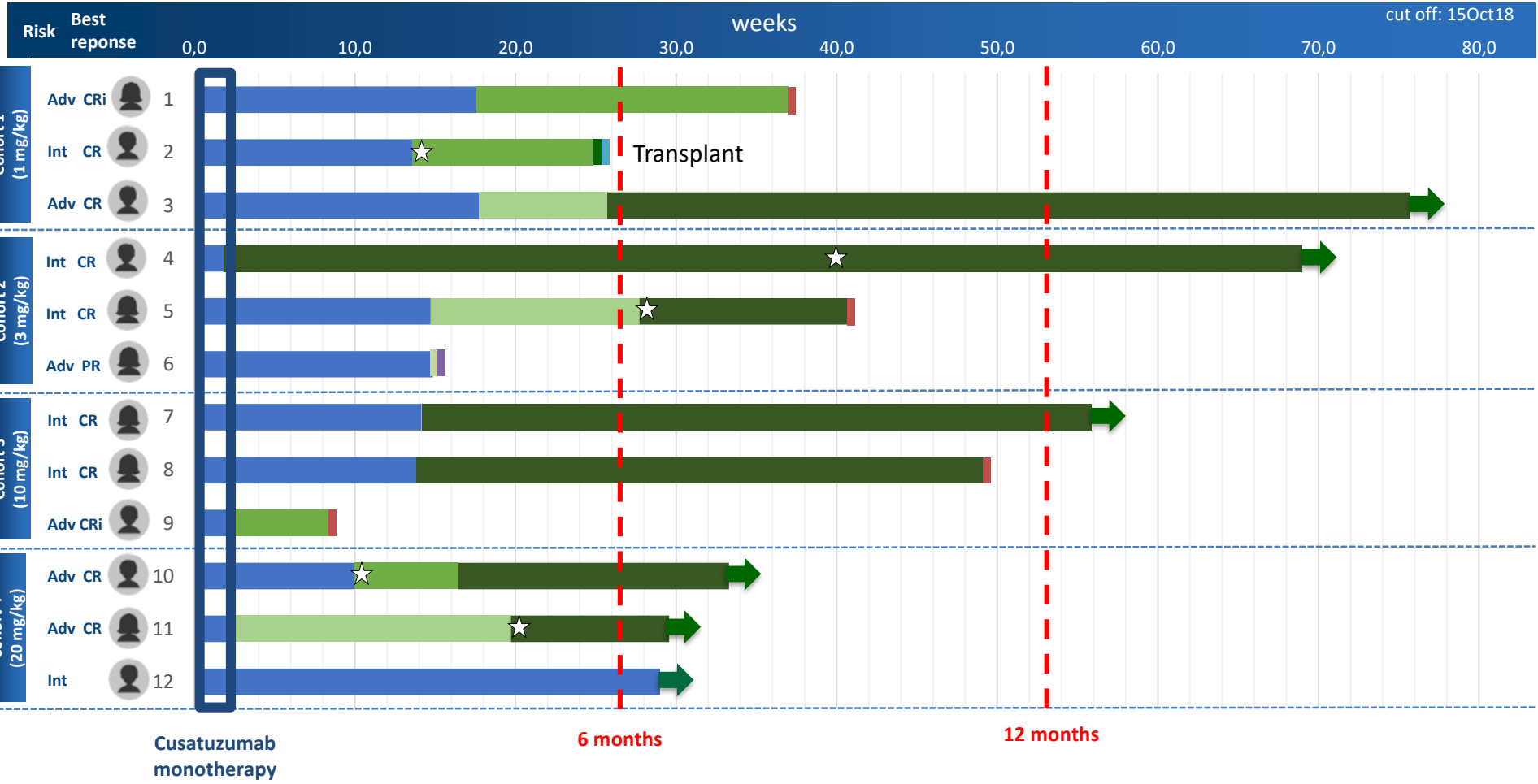
* Grade 3: only if reported in at least 2 cases

- No dose-limiting toxicity observed
- Grade 3 and 4 hematological toxicities in line with expected Vidaza toxicities in 6 patients (50%), predominantly reported in 1 mg/kg and 3 mg/kg cohorts
- Other single cases of Grade 3 events were reported: Constipation, Arthritis, Proctitis, Epistaxis, Tooth Infection, Vulvovaginal Inflammation, Anal Abscess, Agitation, Lung infection, Pleuro-pericarditis, Lung infiltration
- Multi-Organ failure (Grade 5) was due to disease progression

argenx data - Listing 16.2.9.1.1 Treatment-Emergent Adverse Events (TEAE) - Table 14.3.1.2 Treatment-Emergent Adverse Events, by SOC and PT

92% (11/12) Response Rate – CR/CRi/PR

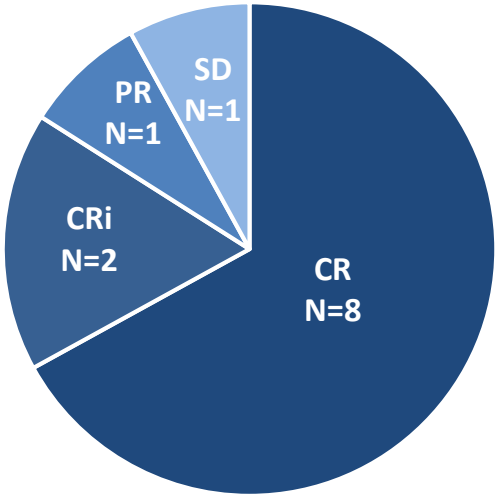
Three patients on study for more than 12 months



Response Rate Skewed Towards CR/CRi (10/12 Patients)

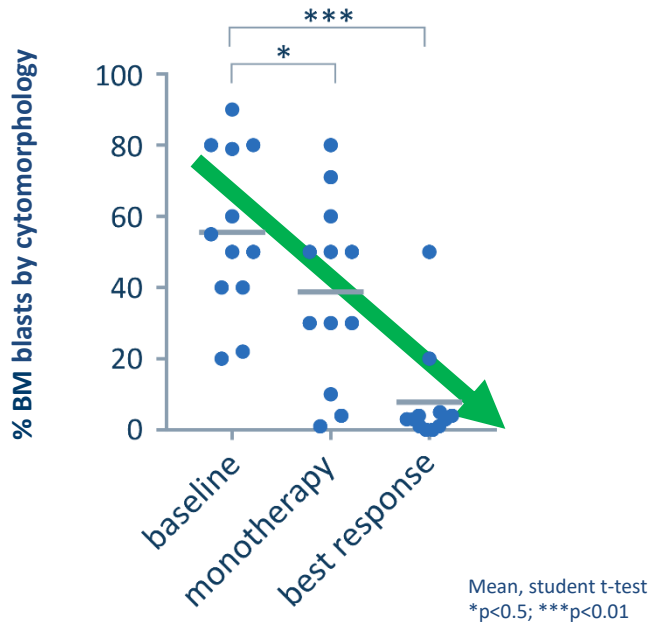
Response correlates with decrease of blasts in bone marrow

Best response



CR: Complete Remission
CRi: CR with incomplete hematological recovery
PR: Partial Remission

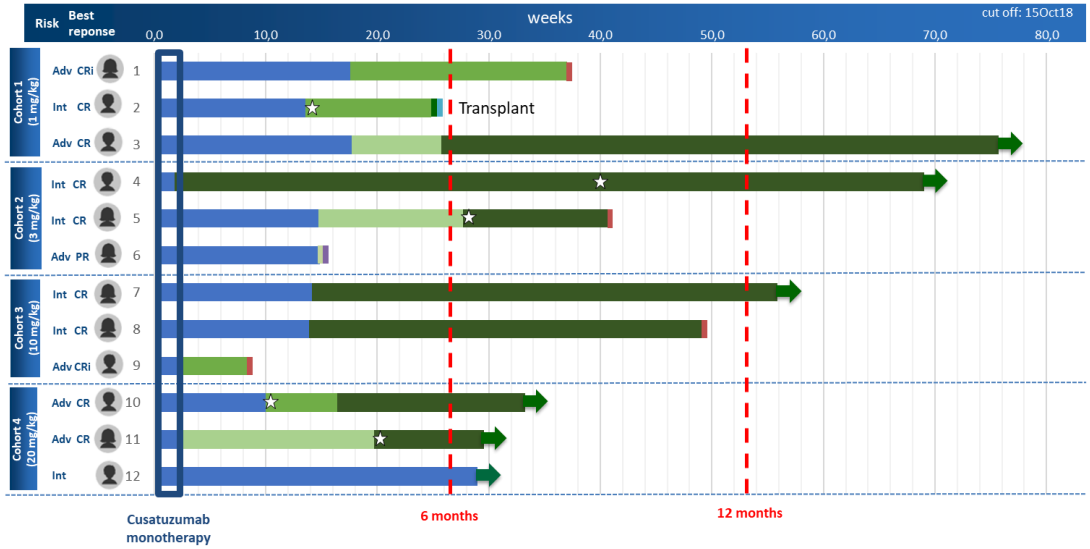
Reduction of blasts in bone marrow



Mean, student t-test
*p<0.5; ***p<0.01

- 11 (92%) patients responded to the combination therapy:
  - Including 10/11 patients reaching complete remission (8 with hematologic recovery and 2 without)
- Mean reduction of bone marrow blasts:
  - 30% after cusatuzumab monotherapy that reduced down to 86% at best response

Rapid Onset of Response with 3 Patients Reaching First Response After Single Dose



Median time to first response

	Weeks/months
All patients	**14.0/3.3**
1 mg/kg	17.6/4.0
3 mg/kg	14.7/3.4
10 mg/kg	13.9/3.2
20 mg/kg	10.0/2.3

Ongoing

MRD - BM by flow and molecular genetics

EOT due to PD

EOT due to AE (Hypotension)

EOT due to transplant

Time to response (weeks)

Partial remission (PR)

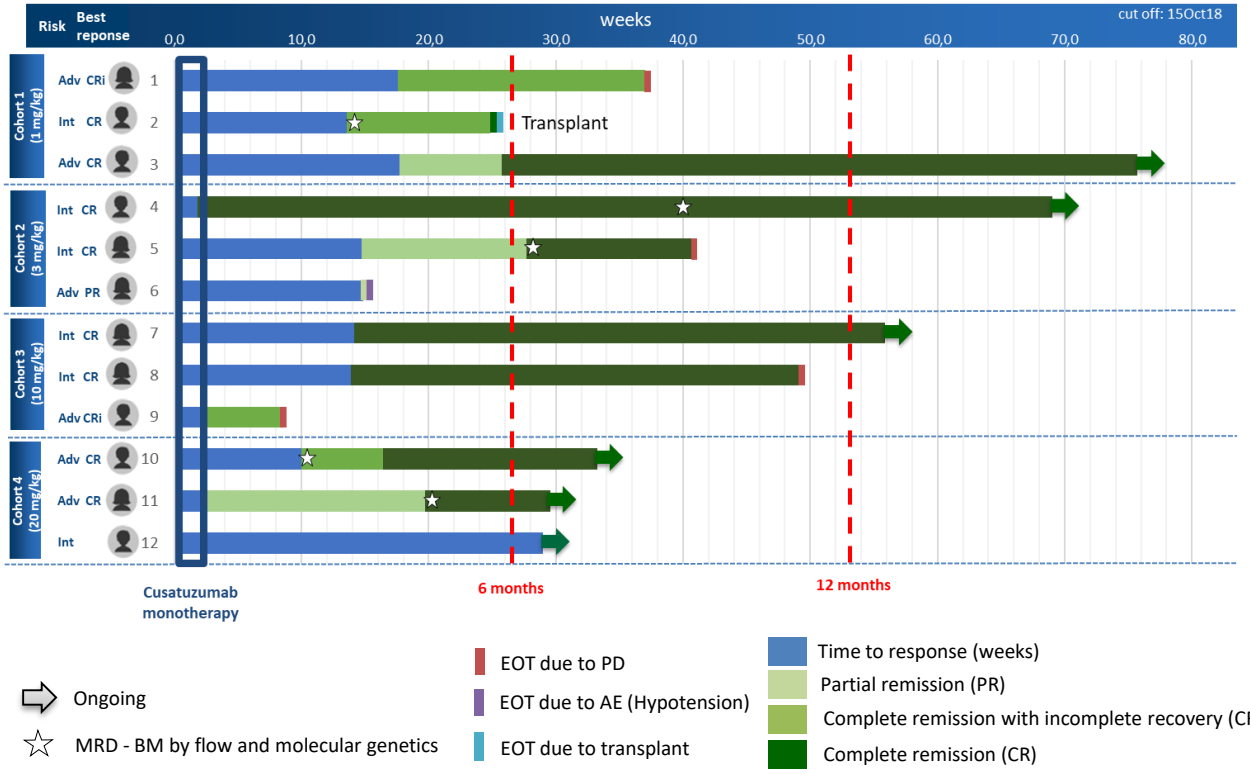
Complete remission with incomplete recovery (CRi)

Complete remission (CR)

- 3 (25%) patients reached a first response after a single dose of cusatuzumab

Duration of Response – Ongoing Analysis

3/12 patients event free survival > 1 year; 6/12 patients still on study



Median duration of response

	Weeks/months
All patients	**23.6/5.5**
1 mg/kg	19.4/4.9
3 mg/kg	26.0/6.1
10 mg/kg	35.3/8.2
20 mg/kg	23.9/5.6

Median event free survival

	Weeks/months
All patients	**35.1/8.1**
1 mg/kg	37.0/8.5
3 mg/kg	40.7/9.3
10 mg/kg	49.0/11.2
20 mg/kg	29.0/6.7

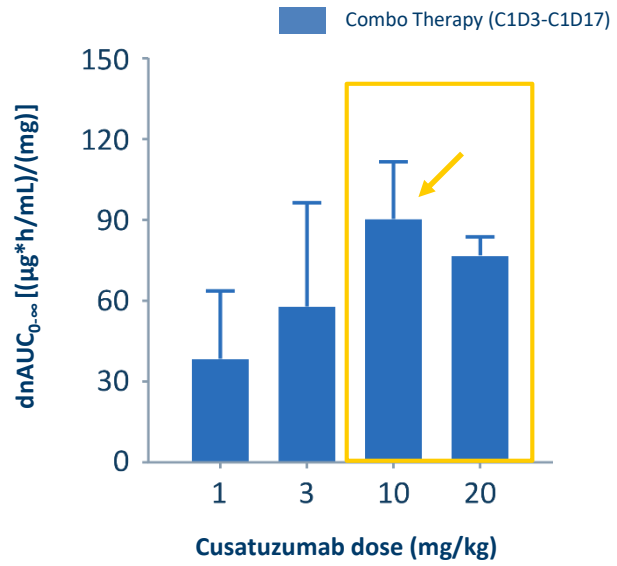
- Median duration of response: 5.5 months
- Median event free survival: 8.1 months (range: 2 months – 17.4 months)
- 9 (75%) patients event free survival for > 6 months
- 6 (50%) patients still on trial:
  - 3 patients more than 1 year on trial
  - 1 patient more than 17 months on trial

Recommended Phase 2 Dose Is 10 mg/kg

Saturating serum level at this dose maintained in bone marrow

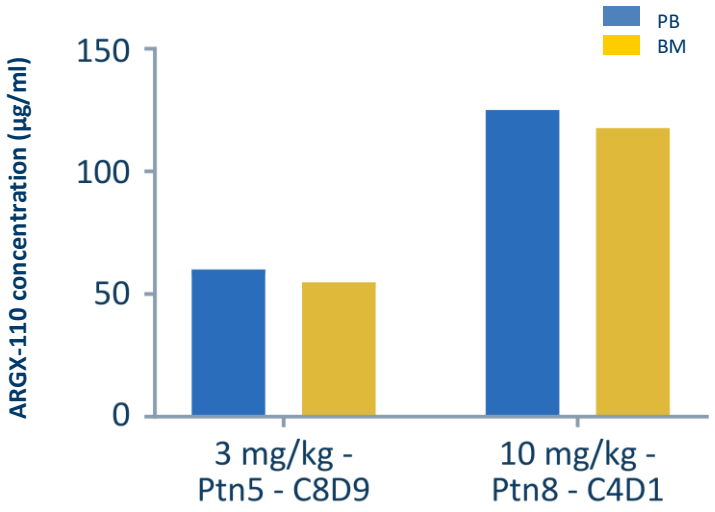
Cusatuzumab blood level saturated from 10 mg/kg

Dose-normalized AUC of cusatuzumab vs dose



Similar level in blood and bone marrow at 10 mg/kg

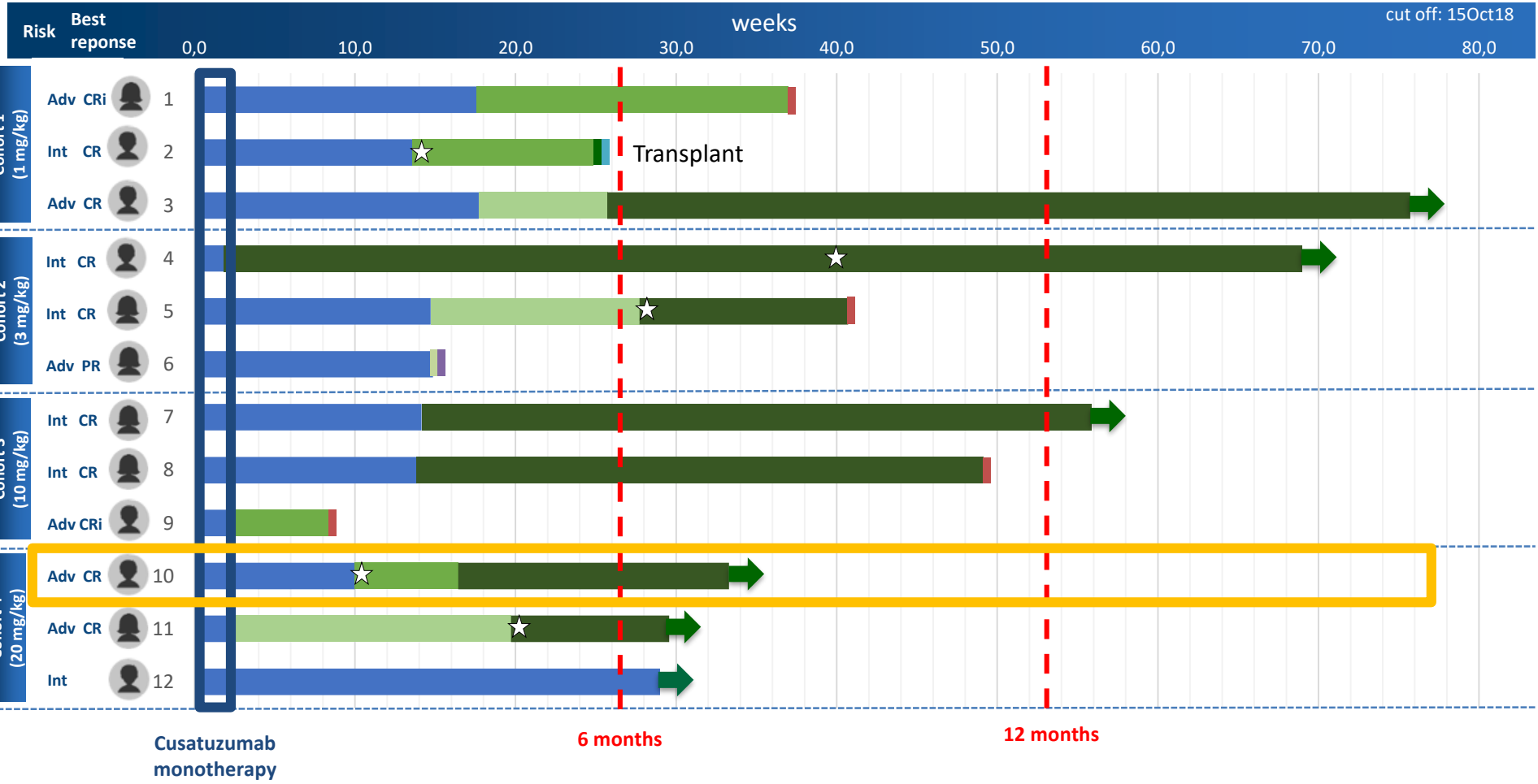
Cusatuzumab level: Peripheral blood vs bone marrow



- RP2D was established at 10 mg/kg based on safety data, pharmacokinetics and saturation of cusatuzumab in blood
- Similar levels of cusatuzumab observed in blood and bone marrow

Patient Case Studies

Case 10: Complete Remission after Lowering Vidaza Concentration

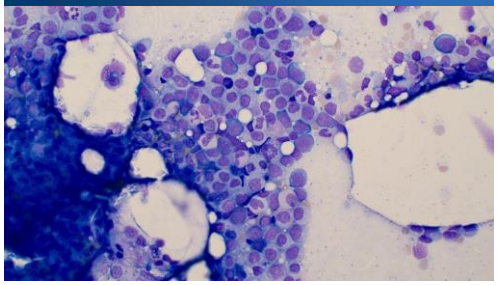


Case 10: Complete Remission after Lowering Vidaza Concentration

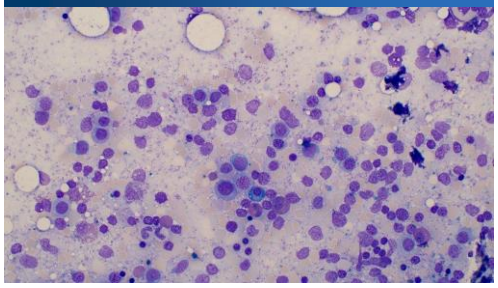
- 77 year old male; AML with myelodysplasia related changes, M2; BM 50% blasts
- Molecular genetics: ASXL1 mutated, RUNX1 mutated, EZH2 mutated, ZRSR2 mutated, SH2B3 mutated; cytogenetics: Deletion 1p; Deletion 7q – Adverse risk profile

Cytomorphology

Screening

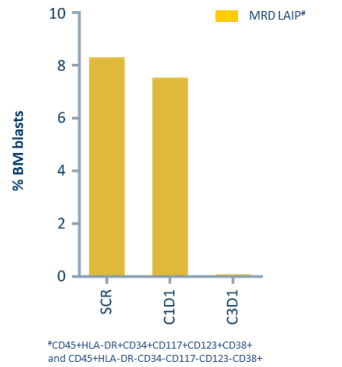


Leukemic clearance (CR) (C3)

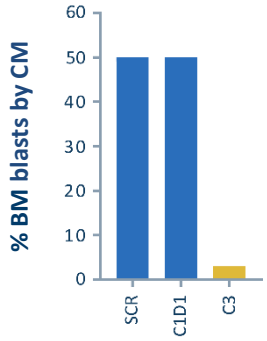


BM aspirate - 40x

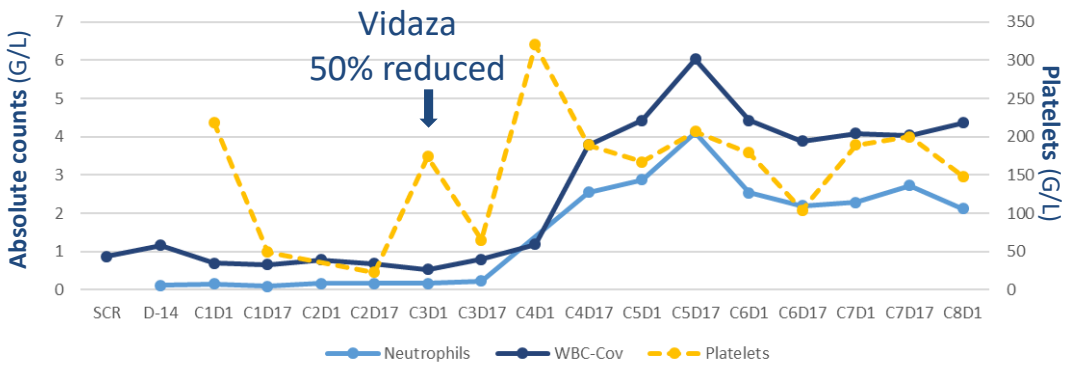
MRD in Bone marrow by flow



% Blasts in bone marrow



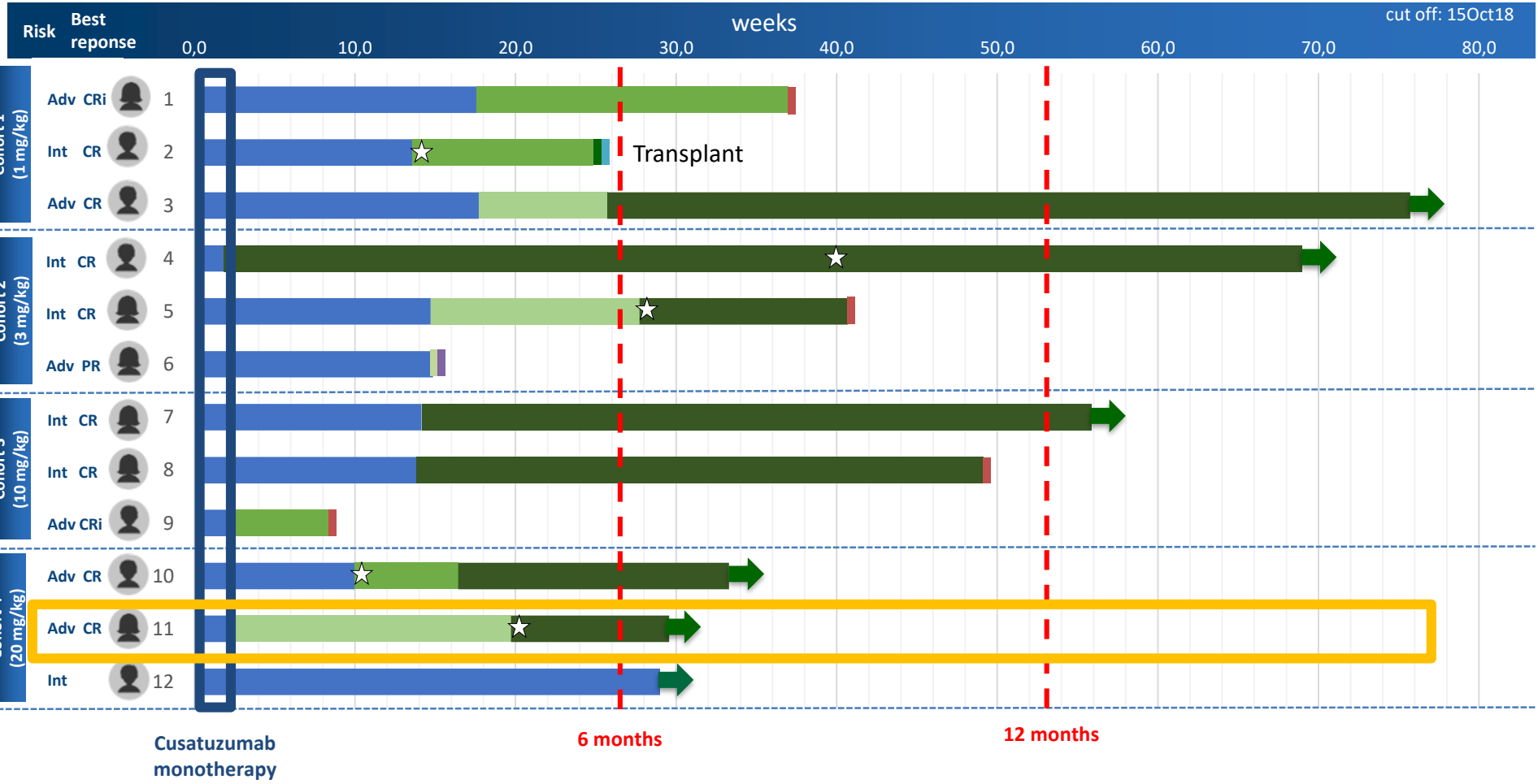
Blood analysis: absolute counts (G/L)



- Complete remission with incomplete hematological recovery at C3 and MRD negativity by flow cytometry
- Complete remission at C4D17
- Vidaza reduced by 50% due to Vidaza hematoxicity (C3); cusatuzumab maintained at 20 mg/kg
- Still on study

Source: argenx data – patient anecdotes – uncleaned data

Case 10: Complete Remission after Lowering Vidaza Concentration

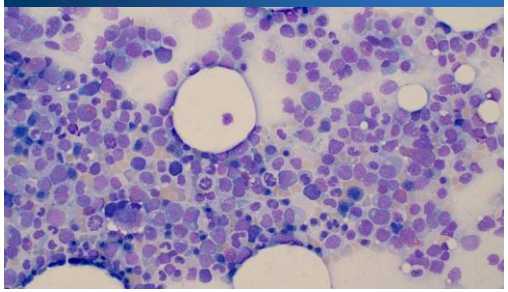


Case 11: Complete Remission in a TP53 Mutant AML Patient

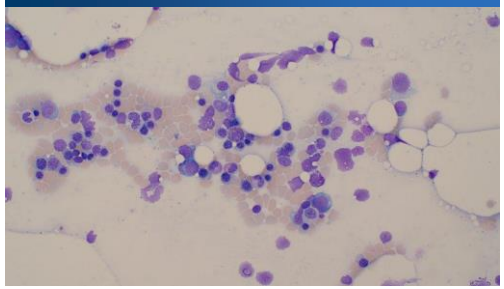
- 72 year old female; AML with myelodysplasia related changes; BM 22% blasts CM
- Molecular genetics: ASXL1 mutation, TP53 mutation; cytogenetics: 46,XX,-7,+mar[14]/46,XX[6] – Adverse risk profile

Cytomorphology

Screening

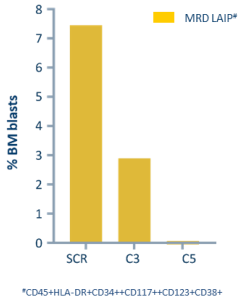


Leukemic clearance (CR) (C5)

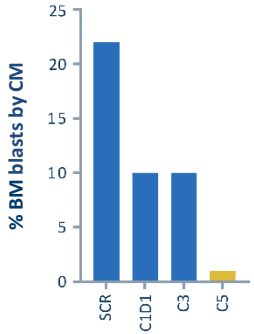


BM aspirate - 40x

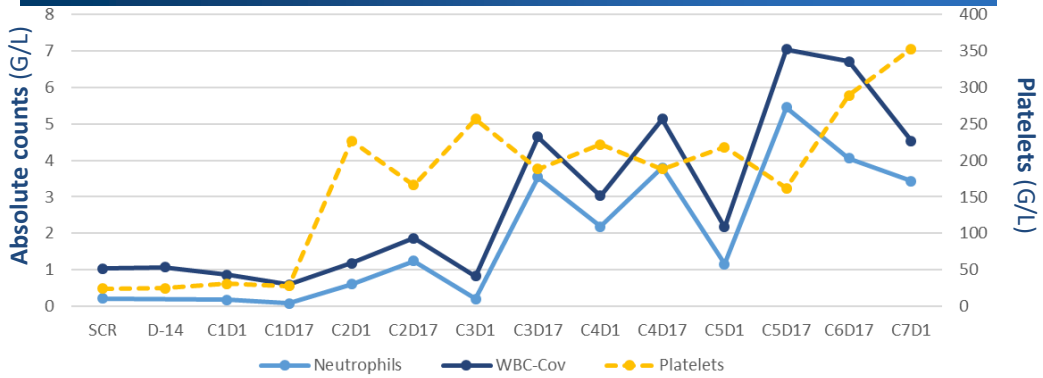
MRD in Bone marrow by flow



% Blasts in bone marrow



Blood analysis: absolute counts (G/L)



- Partial remission at C1 after one dose of 20 mg/kg cusatuzumab monotherapy
- Complete remission at C5 with MRD negativity by flow cytometry
- Still on study

Source: argenx data – patient anecdotes – uncleaned data

MRD Negativity

Measured by flow cytometry and molecular genetics

Cohort	Case	Response	MRD flow BM*	MRD mol BM	MRD flow PB*	MRD mol PB
1 mg/kg	1	CRi	+	+	+	+
	2	CR	-	-	-	-
	3	CR	+	NA	-	NA
3 mg/kg	4	CR	-	-	-	-
	5	CR	+	-	-	+
	6	PR	+	+	+	+
10 mg/kg	7	CR	NA	+	-	NA
	8	CR	+	+	-	+
	9	Cri	+	NA	+	NA
20 mg/kg	10	CR	-	+	-	+
	11	CR	-	+	-	+
	12		+	NA	+	NA

* MRD negativity threshold = 10E-4

Overall Conclusions Phase 1 Dose Escalation

Favorable tolerability profile

- No obvious toxicity on top of Vidaza toxicity
- No dose-limiting toxicity observed

Encouraging proof-of-biology data in 12 patients (4 dose cohorts; 3 pts each)

- 92% response rate (11/12) mainly CR/CRi
- 3 patients responded after cusatuzumab monotherapy
- Significant blast reduction in bone marrow after cusatuzumab monotherapy
- MRD negativity in 42% (5/12) treated patients

Supported by **translational dataset**

- Decreased sCD27 levels
- Reduced LSC colony formation
- Increased myeloid differentiation – asymmetric division

Recommended Phase 2 dose: 10 mg/kg

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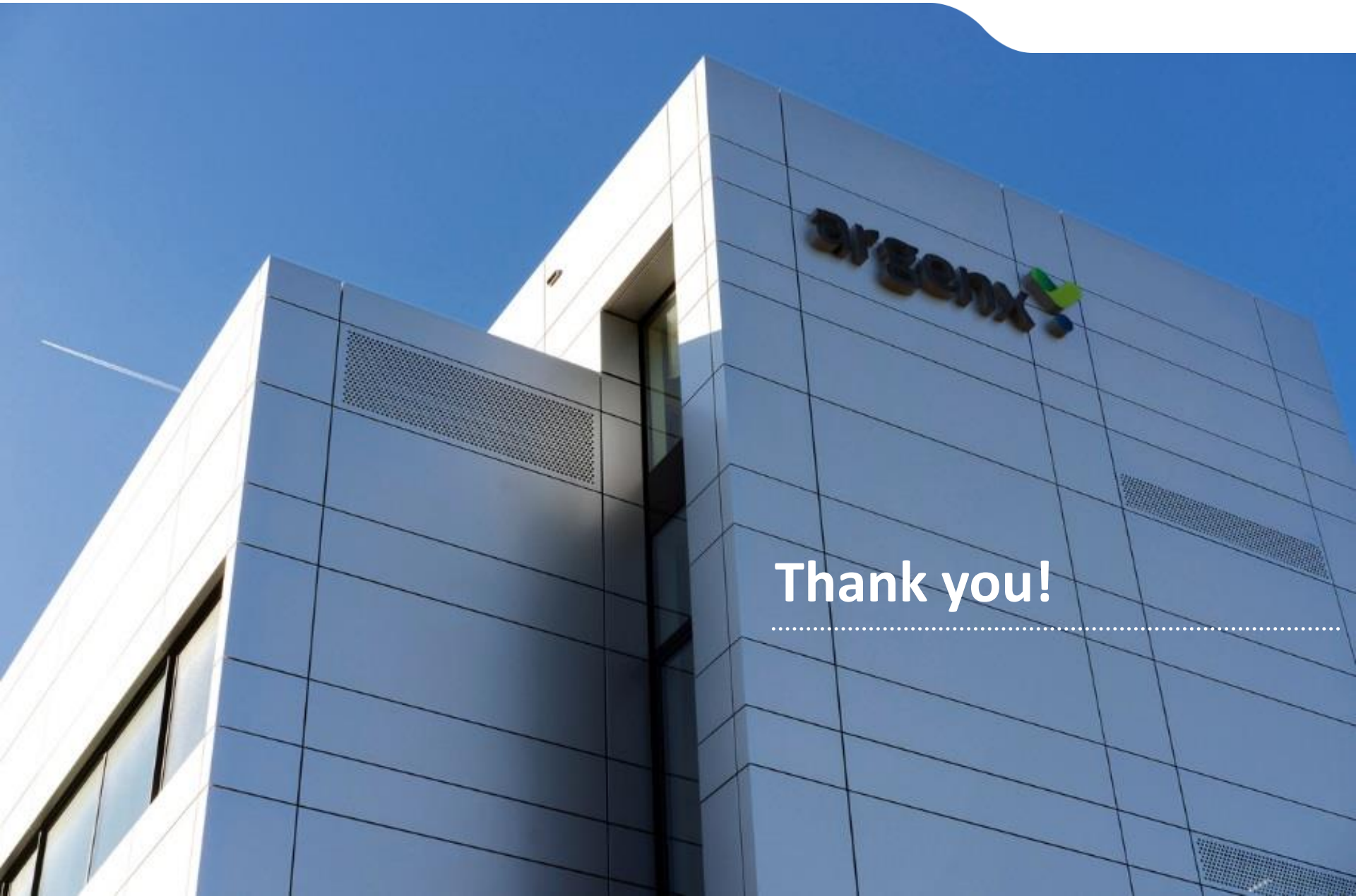

Thank you!