Analysis of Efficacy and Safety of Loncastuximab Tesirine (ADCT-402) by Demographic and Clinical Characteristics in Relapsed/Refractory Diffuse Large B-Cell Lymphoma

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15th International Conference on Malignant Lymphoma

June 18–22, 2019, Lugano, Switzerland

Conflict of Interest Disclosures

John Radford

Consultant or advisory role: ADC Therapeutics, Novartis, Seattle Genetics, Takeda

Stock ownership: AstraZeneca, GSK (spouse)

Honoraria: ADC Therapeutics, Takeda

Research funding: Takeda

Other renumeration: *Travel/miscellaneous expenses:* ADC Therapeutics, Takeda

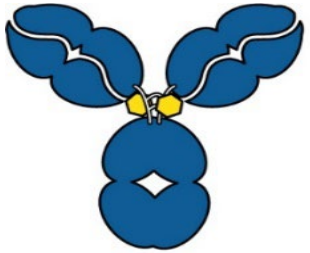
Acknowledgments

The authors would like to thank all the participating patients and their families, all study co-investigators, and research coordinators

Study sponsored by ADC Therapeutics SA (NCT02669017)

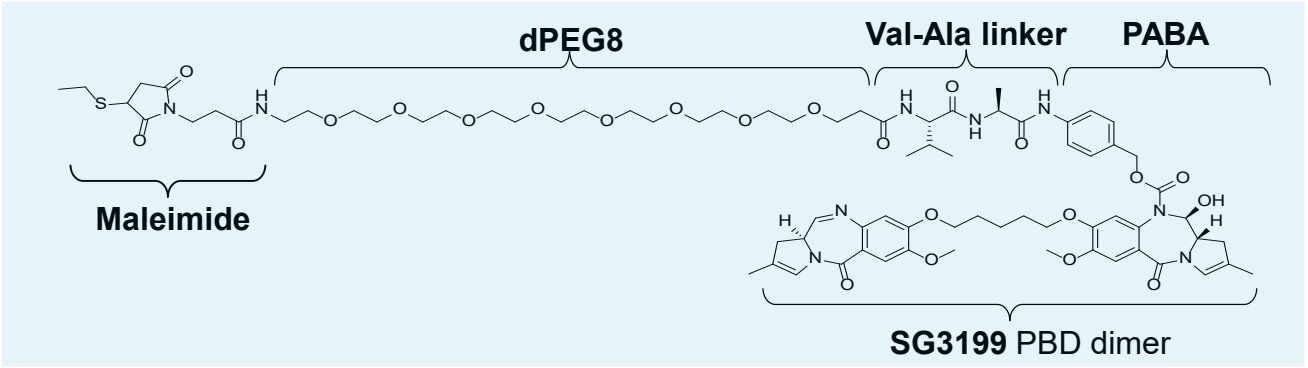
Editorial support was provided by Fishawack Communications Ltd.

Loncastuximab Tesirine (ADCT-402)



Anti-CD19 Ab

Tesirine/ SG3249



Loncastuximab tesirine comprises a humanized anti-CD19 Ab stochastically conjugated to a potent PBD dimer toxin[1]

The majority of B-cell malignancies express CD19 at normal to high levels[2]

1. **Loncastuximab tesirine binds to CD19 antigen on the tumour cell surface**
2. **ADC is internalized, the linker is cleaved, and PBD dimers are released**
3. **Cytotoxic DNA cross-link formation**
4. **Stalled DNA replication fork**
5. **Cell goes into apoptosis**

1. Zammarchi F, et al. *Blood*. 2018;131:1094–105. 2. Wang K, et al. *Exp Hematol Oncol*. 2012;1:36.

Ab, antibody; ADC, antibody drug conjugate; CD19, cluster of differentiation 19; PABA, para-aminobenzoic acid; PBD, pyrrolobenzodiazepine; Val-Ala, valine-alanine.

Loncastuximab Tesirine Phase 1 Study in NHL

R/R B-cell NHL
failed, or intolerant to, any established therapy

1-hour intravenous infusion (15–200 µg/kg)
Day 1 (Q3W)
Dose escalation: 3+3 design
(Cycle 1 dose-limiting toxicity observation period)

First-in-human study of loncastuximab tesirine in patients with R/R B-cell NHL (NCT02669017)

- **Part 1 (dose escalation)**: Evaluate safety and tolerability and determine the recommended dose for dose expansion (Part 2)
- **Part 2 (dose expansion)**: Evaluate safety and tolerability at recommended doses (120 µg/kg and 150 µg/kg)

Enrollment, treatment, and follow-up complete

Loncastuximab tesirine demonstrated encouraging and durable single-agent antitumour activity and manageable toxicity at doses ≥120 µg/kg in patients with R/R DLBCL

This presentation focuses on subgroup analyses of response to loncastuximab tesirine at doses ≥120 µg/kg in patients with R/R DLBCL by demographic and clinical characteristics

DLBCL, diffuse large B-cell lymphoma; Q3W, every 3 weeks; NHL, non-Hodgkin lymphoma; R/R, relapsed/refractory.

Baseline Characteristics of Patients With DLBCL (Safety Analysis Set: Dose ≥120 µg/kg; N=129)

Patient Characteristic		Total (N=129)
Sex, n (%)	Male	77 (59.7)
	Female	52 (40.3)
Age group, n (%)	<65 Years	69 (53.5)
	65–74 Years	36 (27.9)
	≥75 Years	24 (18.6)
Bulky disease, n (%)		19 (14.7)
Double/Triple hit, n (%)		22 (17.1)
Transformed, n (%)		33 (25.6)
ECOG performance status, n (%)	0	31 (24.0)
	1	81 (62.8)
	2	15 (11.6)
	3	2 (1.6)

Patient Treatment History		Total (N=129)
First-line chemotherapy response, n (%)	Relapsed	82 (63.6)
	Refractory	26 (20.2)
	Other*	21 (16.3)
Last-line chemotherapy response, n (%)	Relapsed	44 (34.1)
	Refractory	76 (58.9)
	Other*	9 (7.0)
Number of previous systemic therapies, n (%)	≤3	80 (62.0)
	>3	49 (38.0)

All data presented are for patients with R/R DLBCL treated with ≥120 µg/kg of loncastuximab tesirine

Data shown as of Oct 16, 2018. *Other: missing/not evaluable.
DLBCL, diffuse large B-cell lymphoma; ECOG, Eastern Cooperative Oncology Group; R/R, relapsed/refractory.

TEAEs of Any Grade in ≥20% of Patients (Safety Analysis Set; N=129)

TEAEs, n (%)	Total (N=129)
Patients with any TEAE	128 (99.2)
Platelet count decreased*	88 (68.2)
Neutrophil count decreased*	75 (58.1)
Fatigue	55 (42.6)
Peripheral oedema	44 (34.1)
Nausea	44 (34.1)
Anaemia	40 (31.0)
Gamma-glutamyltransferase increased	37 (28.7)
Rash	35 (27.1)
Constipation	31 (24.0)
Dyspnoea	30 (23.3)
Pleural effusion	28 (21.7)
Decreased appetite	26 (20.2)

The most common grade ≥3 TEAEs (≥10%) were:

- **Gamma-glutamyltransferase increased (20.2%)**
- **Haematologic abnormalities:**
  - **Neutrophil count decreased (38.0%)**
  - **Platelet count decreased (27.1%)**
  - **Anaemia (11.6%)**

Data shown as of Oct 16, 2018. Purple shading indicates hematologic abnormalities and green shading indicates features of fluid retention.
*Data on platelet count and neutrophil count decreases are based on laboratory abnormality reporting. TEAE, treatment-emergent adverse event.

TEAEs of Any Grade in ≥20% of Patients: By Age Group (Safety Analysis Set; N=129)

TEAEs (Any Grade), n (%)	Age Group			
	<65 Years (n=69)	65–74 Years (n=36)	≥75 Years (n=24)	Total (N=129)
Patients with any TEAE	69 (100.0)	35 (97.2)	24 (100.0)	128 (99.2)
Platelet count decreased*	50 (72.5)	23 (63.9)	15 (62.5)	88 (68.2)
Neutrophil count decreased*	39 (56.5)	23 (63.9)	13 (54.2)	75 (58.1)
Fatigue	22 (31.9)	18 (50.0)	15 (62.5)	55 (42.6)
Peripheral oedema	17 (24.6)	14 (38.9)	13 (54.2)	44 (34.1)
Nausea	27 (39.1)	12 (33.3)	5 (20.8)	44 (34.1)
Anaemia	24 (34.8)	11 (30.6)	5 (20.8)	40 (31.0)
GGT increased	25 (36.2)	7 (19.4)	5 (20.8)	37 (28.7)
Rash	20 (29.0)	6 (16.7)	9 (37.5)	35 (27.1)
Constipation	13 (18.8)	12 (33.3)	6 (25.0)	31 (24.0)
Dyspnoea	12 (17.4)	11 (30.6)	7 (29.2)	30 (23.3)
Pleural effusion	10 (14.5)	9 (25.0)	9 (37.5)	28 (21.7)
Decreased appetite	16 (23.2)	6 (16.7)	4 (16.7)	26 (20.2)

Data shown as of Oct 16, 2018. Purple and green shading indicate hematologic abnormalities and features of fluid retention, respectively. *Data on platelet count and neutrophil count decreases are based on laboratory abnormality reporting. GGT, gamma-glutamyltransferase; TEAE, treatment-emergent adverse event.

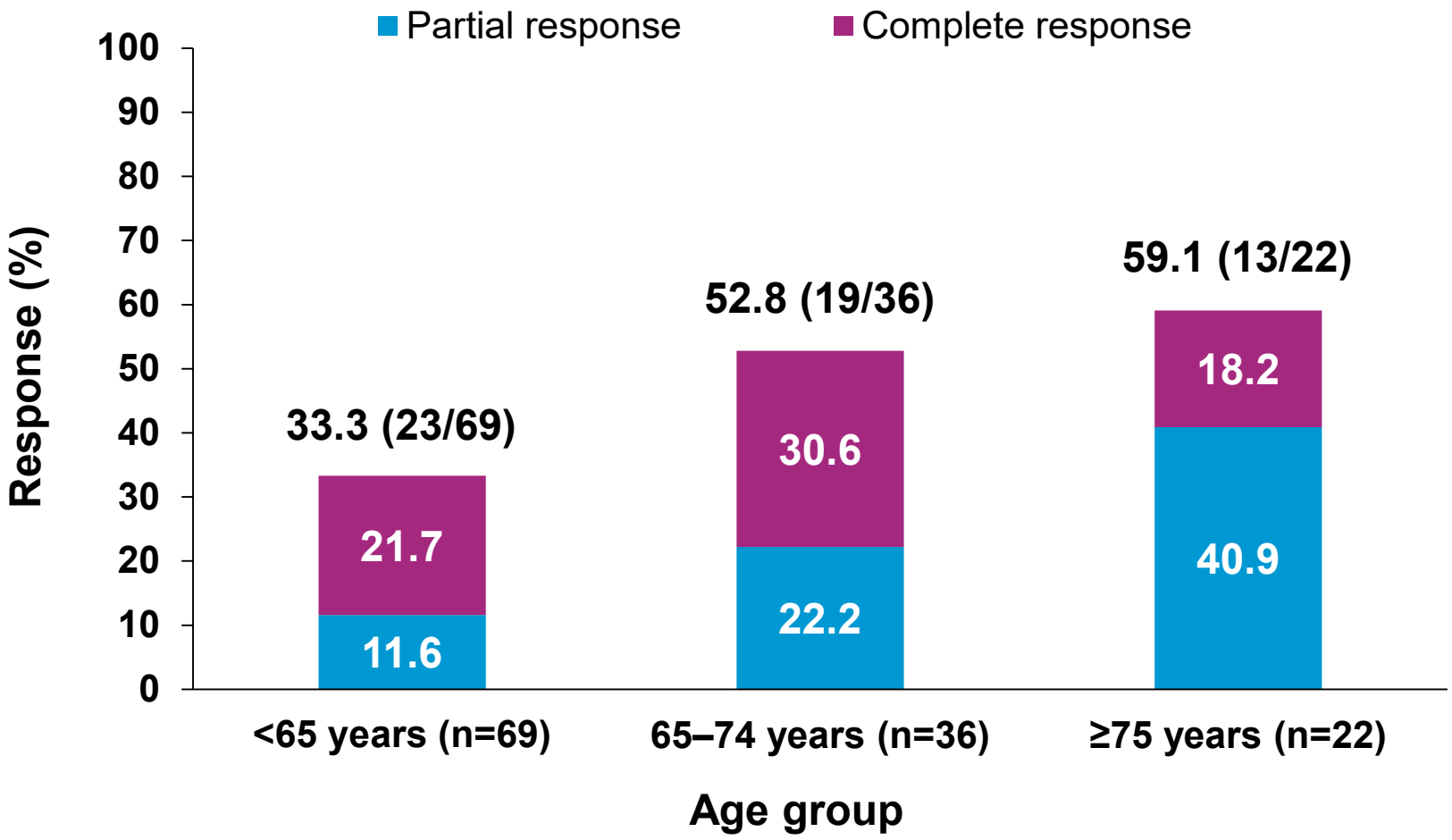
Overall Response Rate: By Clinical Characteristics

Characteristic	Subgroup	All ≥120 µg/kg, % (responders/total)
Age group	<65 Years	33.3 (23/69)
	65–74 Years	52.8 (19/36)
	≥75 Years	59.1 (13/22)
Bulky disease	Absent	46.8 (51/109)
	Present	22.2 (4/18)
Double/Triple hit	Absent	47.6 (50/105)
	Present	22.7 (5/22)
Transformed	No	39.6 (38/96)
	Yes	54.8 (17/31)

Characteristic	Subgroup	All ≥120 µg/kg, % (responders/total)
Number of prior therapies	≤3 lines	43.8 (35/80)
	>3 lines	42.6 (20/47)
Response to first-line therapy	Relapsed	53.1 (43/81)
	Refractory	23.1 (6/26)
Response to most recent therapy	Relapsed	59.1 (26/44)
	Refractory	35.1 (26/74)
Overall		**43.3 (55/127)**

Data shown as of Oct 16, 2018.

Overall Response Rate: By Age Group (Efficacy Analysis Set; N=127)



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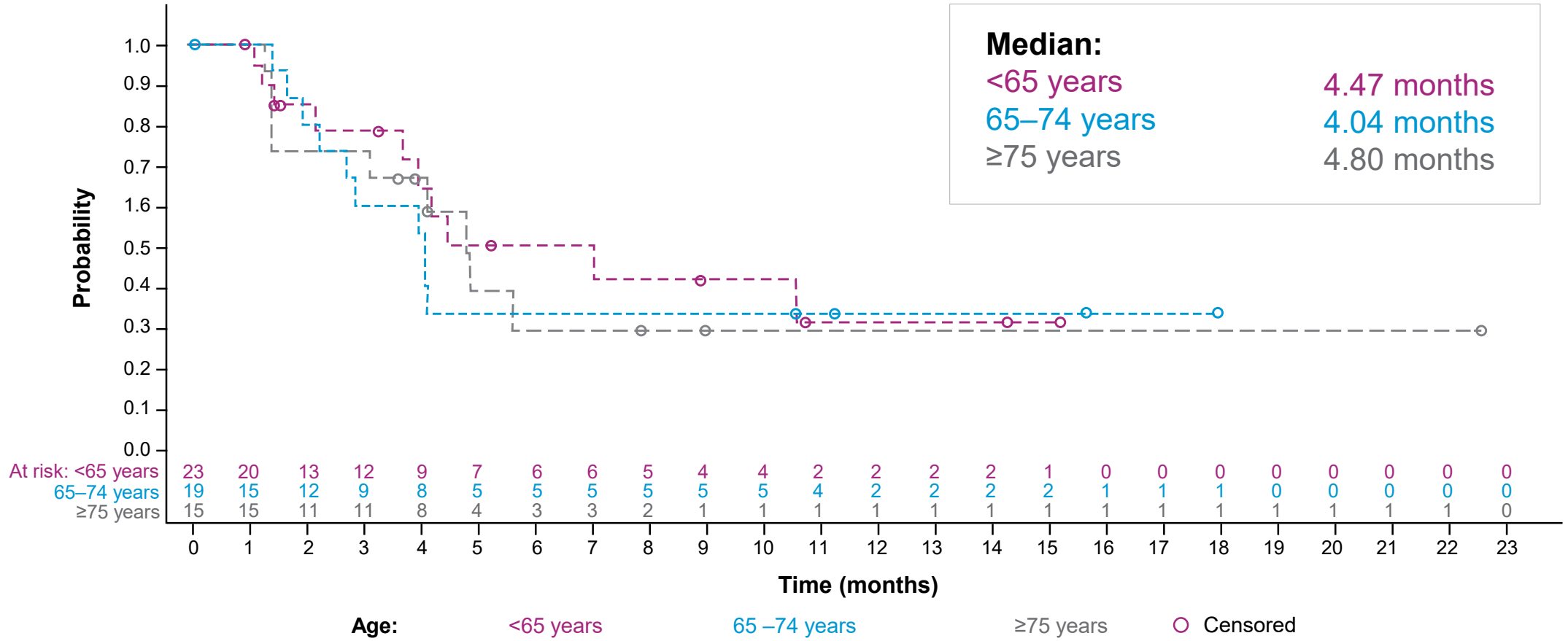
Duration of Response: By Age Group (Efficacy Analysis Set; N=127)



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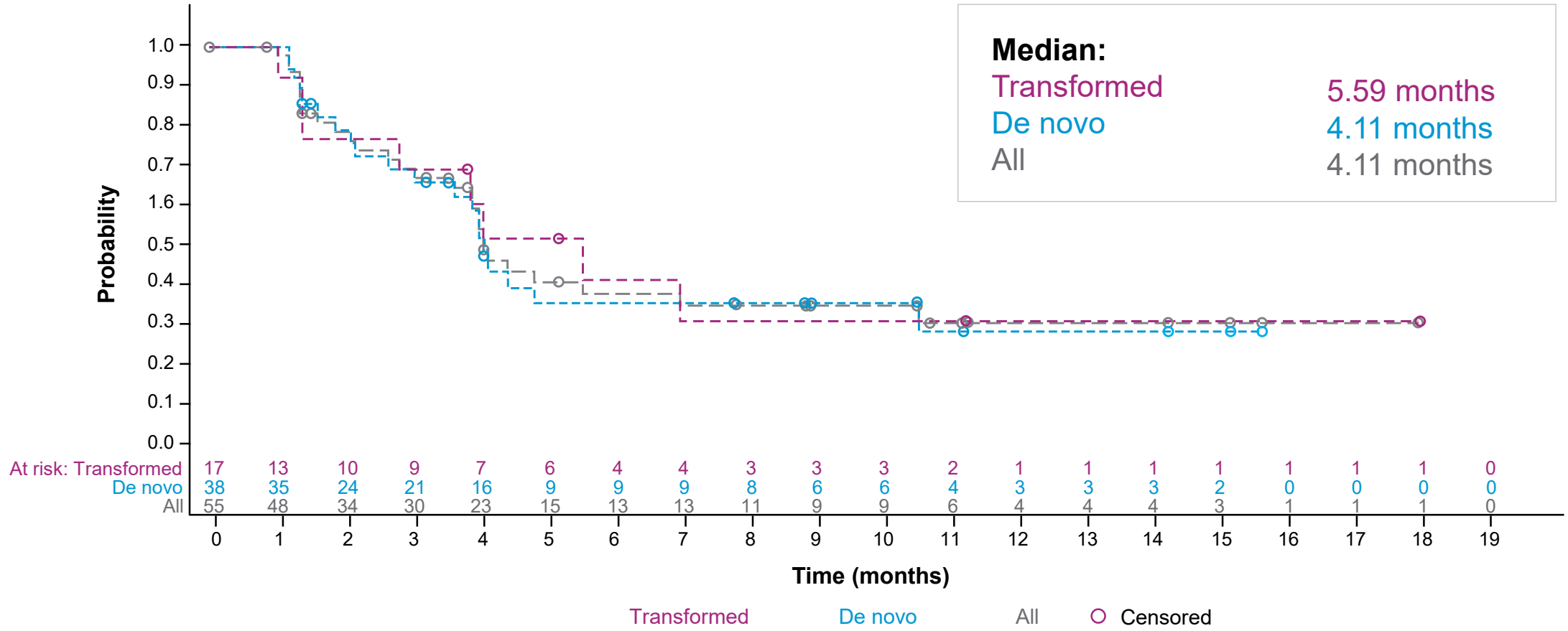
Duration of Response: By Transformed vs De Novo DLBCL (Efficacy Analysis Set; N=127)



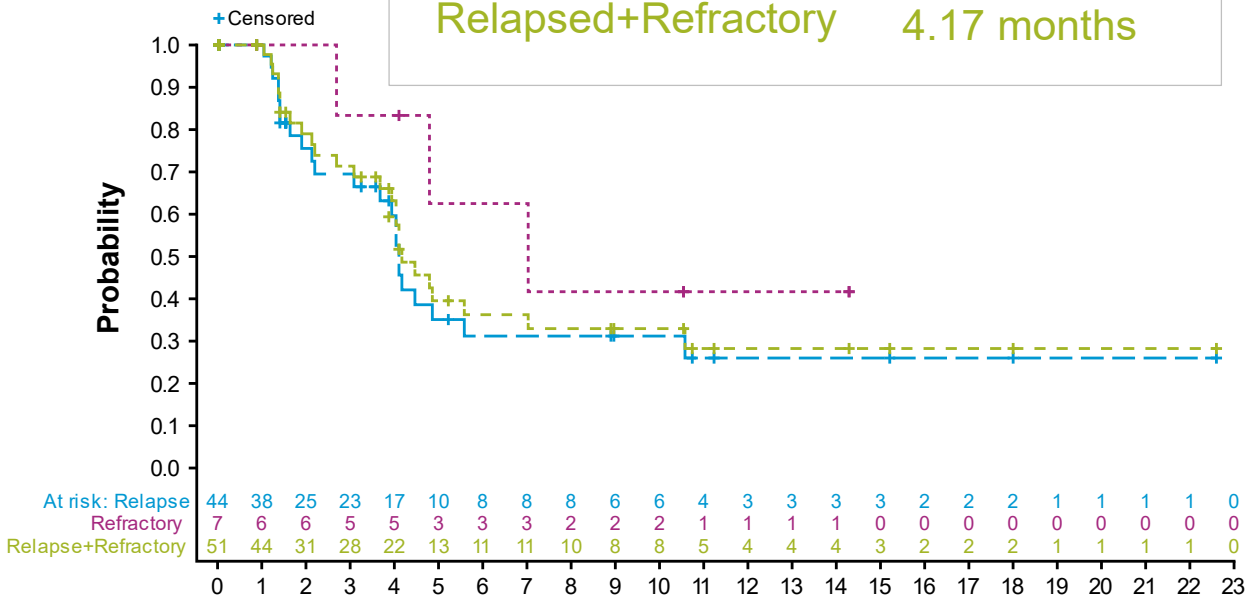
Data shown as of Oct 16, 2018. DLBCL, diffuse large B-cell lymphoma.

Duration of Response: By Response to Previous Therapy

Response to first-line therapy

Median:

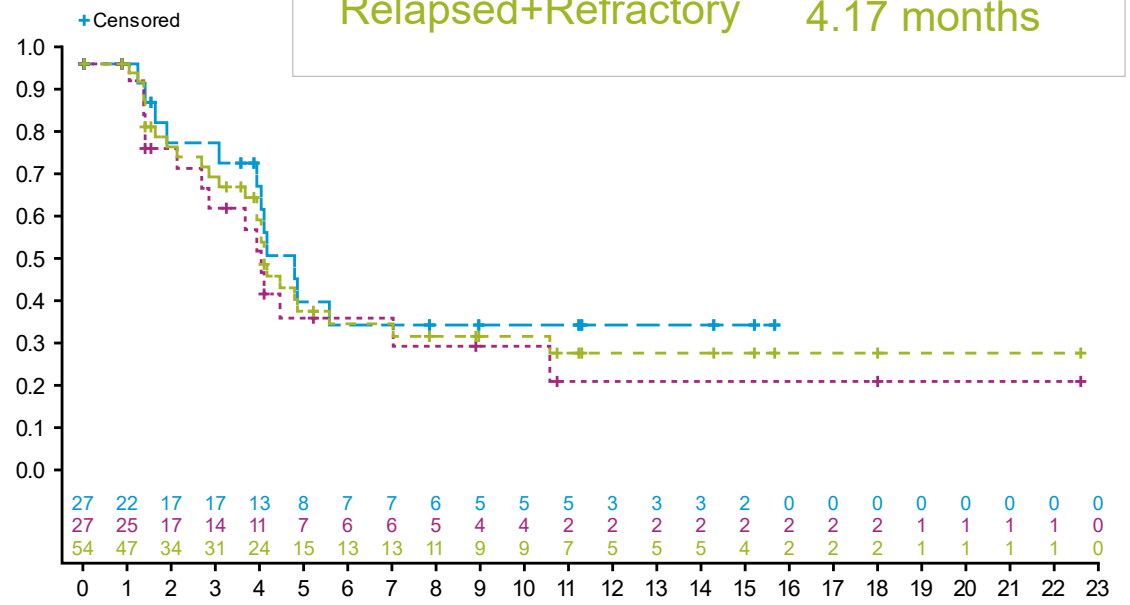
Relapsed	4.11 months
Refractory	7.03 months
Relapsed+Refractory	4.17 months



Response to most recent therapy

Median:

Relapsed	4.80 months
Refractory	4.11 months
Relapsed+Refractory	4.17 months



Time (months)

Response Category: Relapsed Refractory Relapsed+Refractory

Data shown as of Oct 16, 2018.

Summary

Loncastuximab tesirine at doses ≥120 µg/kg has encouraging antitumour activity with an acceptable safety profile in patients with R/R DLBCL

Subgroup analyses showed that:

- **Older patients tolerated loncastuximab tesirine and had an encouraging ORR**
- **Patients with transformed disease also had an encouraging ORR to loncastuximab tesirine**
- **Patients with ≥3 prior lines of therapy had a comparable ORR to patients with <3 prior lines of therapy**
- **Patients with refractory DLBCL had lower ORR than patients with relapsed DLBCL but durable responses were observed**

DLBCL, diffuse large B-cell lymphoma; ORR, overall response rate; R/R, relapsed/refractory.