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# Current results with Camidanlumab Tesirine (Cami) in Hodgkin Lymphoma

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# Disclosures

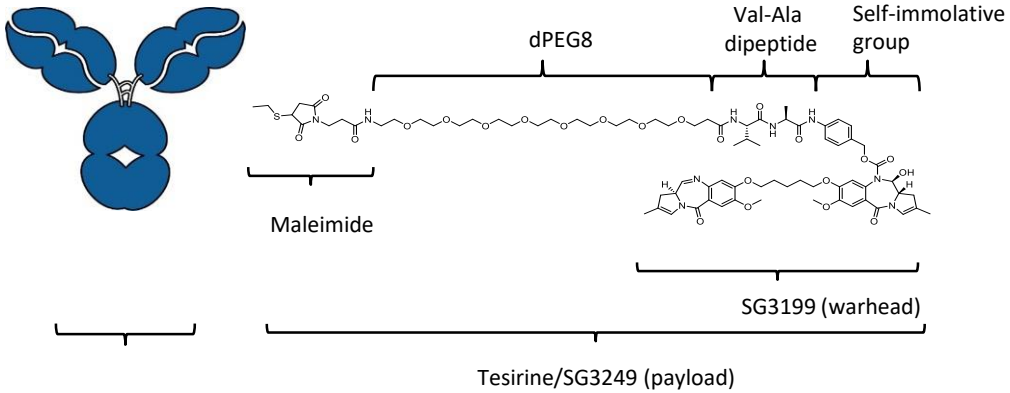
I have received honoraria from:

Takeda, Roche, ADC Therapeutics, Beigene, Incyte, MSD, Pfizer, Daiichi Sankyo, Gilead, Novartis, Celgene, Astra Zeneca

I have received research funding from:

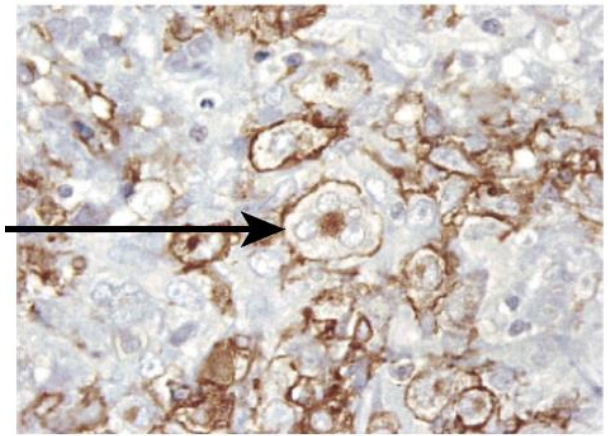
BMS, MSD, Amgen, Pfizer, Beigene

# Camidanlumab tesirine




Immunological rationale

- Targeting of CD25+ Tregs may increase the Teff:Treg → immunological tumor eradication
- Anti-CD25 therapies synergize with PD-1 blockade to eradicate established tumors



From: Janik *et al* (2015) PNAS

Mode of action

1. Cami binds to the CD25 antigen on the tumor cell surface
2. ADC internalization, linker cleavage and PBD release
3. Cytotoxic DNA cross-link formation
4. Stalled DNA replication fork causing cell death cell death

# Phase 1 in HL and NHL

**Histologically confirmed relapsed/refractory NHL* or HL**
*Including Stage ≥Ib Cutaneous T-cell Lymphoma

2-part study:
- *Part 1*: Dose escalation: continual reassessment method;
- *Part 2*: Dose expansion(s)

1-hour intravenous infusion (3–300 µg/kg); Day 1 every 3 weeks

**PRIMARY OBJECTIVE:** Safety and tolerability and determine the MTD / RDE of camidanlumab tesirine

**SECONDARY OBJECTIVES:** Pharmacokinetic profile of camidanlumab tesirine
Clinical activity of camidanlumab tesirine as measured by ORR, DoR, PFS, and OS

For **HL population: MTD was not reached; 2 RDEs** for Part 2 were identified as **30 and 45 µg/kg Q3W**
For **NHL population**: Data were presented at this meeting in **Poster 1658[1] on Saturday, December 1**

DoR, duration of response; HL, Hodgkin lymphoma; MTD, maximum tolerated dose; NHL, non-Hodgkin lymphoma; ORR, overall response rate; OS, overall survival; PFS, progression-free survival; RDE, recommended dose for expansion

1. Collins GP, *et al*. 60th American Society of Hematology Annual Meeting & Exposition, December 1–4, 2018, San Diego, CA, USA. **Poster 1658**

Hamadani *et al* (2018) ASH oral presentation

# Baseline characteristics

| Patient characteristic | Total (N=67) |
|---|---|
| **Sex, n (%)** | |
| Male | 40 (59.7) |
| Female | 27 (40.3) |
| **Race, n (%)** | |
| White | 55 (82.1) |
| Black or African American | 4 (6.0) |
| Asian | 3 (4.5) |
| Other | 5 (7.5) |
| **Age, years, median (min, max)** | 38.0 (19, 80) |
| **Number of previous systemic therapies, median (min, max)** | **5.0 (2, 15)** |
| Prior brentuximab vedotin (BV), n (%) | 65 (97.0) |
| Prior checkpoint inhibitor (CHPi), n (%) | 47 (70.1) |
| Prior BV and CHPi, n (%) | 47 (70.1) |
| Prior stem cell transplantation, n (%) | 40 (59.7) |
| • Allogeneic stem cell transplantation, n (%) | 7 (10.4) |

Hamadani *et al* (2018) ASH oral presentation

# Selected toxicities summary

| Potentially PBD-related toxicities (SMQ) | Dose (µg/kg) | | | | | |
|---|---|---|---|---|---|---|
| | ≤20 (n=3) | 30 (n=10) | 45 (n=37) | 60 (n=12) | ≥80 (n=5) | Total (N=67) |
| Edema or effusion | 1 (33.3) | 3 (30.0) | 10 (27.0) | 2 (16.7) | 1 (20.0) | 17 (25.4) |
| Skin related | 1 (33.3) | 9 (90) | 25 (67.6) | 10 (83.3) | 4 (80.0) | 49 (73.1) |
| Liver function test | 3 (100) | 1 (10.0) | 13 (35.1) | 8 (66.7) | 4 (80.0) | 29 (43.3) |
| **Selected autoimmune toxicities** | | | | | | |
| Guillain–Barré syndrome/Radiculopathy | 0 (0) | 1 (10.0) | 3 (8.1) | 1 (8.3) | 0 (0) | 5 (7.5) |
| Colitis | 1 (33.3) | 0 (0) | 1 (2.7) | 0 (0) | 0 (0) | 2 (3.0) |
| Hypothyroidism | 0 (0) | 0 (0) | 2 (5.4) | 1 (8.3) | 1 (20.0) | 4 (6.0) |
| Hyperthyroidism | 0 (0) | 0 (0) | 2 (5.4) | 0 (0) | 0 (0) | 2 (3.0) |
| Thyroiditis | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 1 (20.0) | 1 (1.5) |

**TEAEs leading to treatment discontinuation occurred in 19/67 (28.4%) patients**

PBD, pyrrolobenzodiazepine; SMQ, standardised MedDRA query; TEAEs, treatment-emergent adverse events

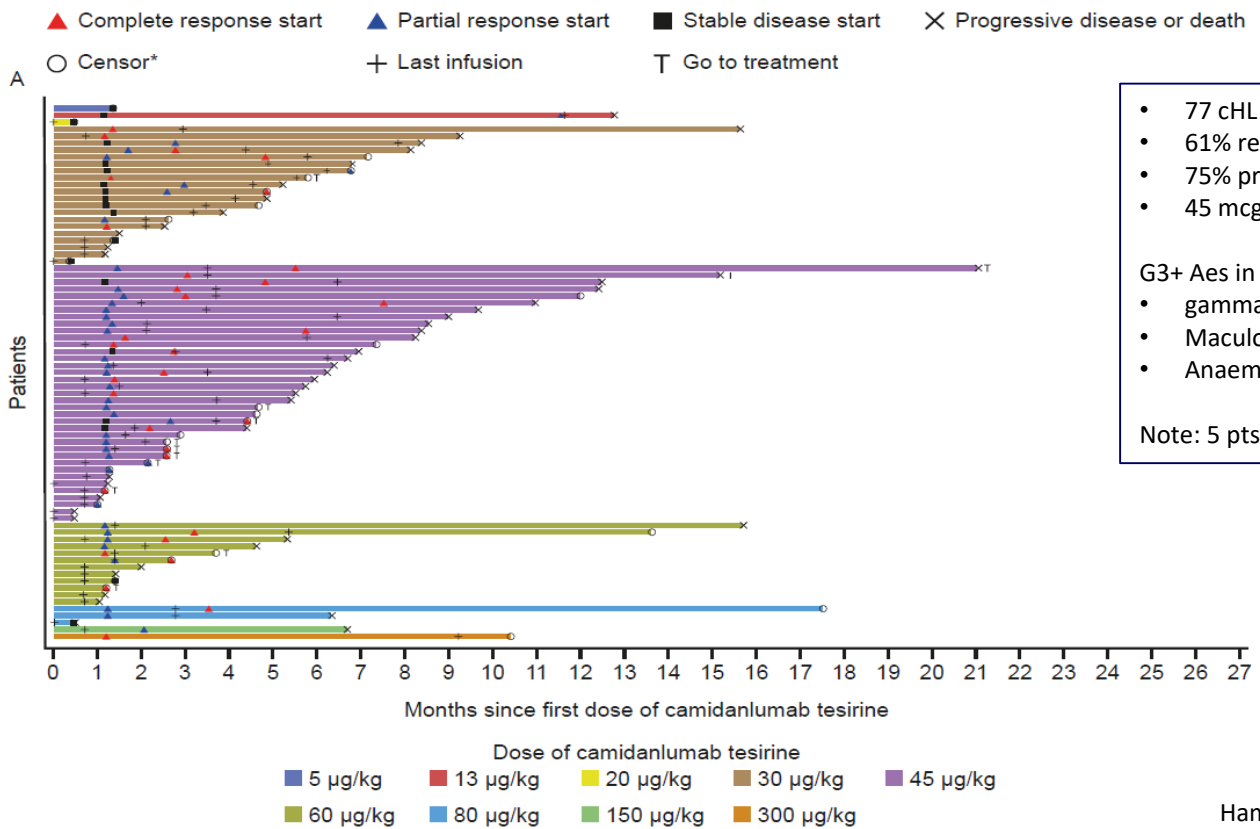
Hamadani *et al* (2018) ASH oral presentation

# Response rates

| Response*, n (%) | Dose (µg/kg) | | | | | |
|---|---|---|---|---|---|---|
| | ≤20 (n=3) | 30 (n=10) | 45 (n=37) | 60 (n=12) | ≥80 (n=5) | Total (N=67) |
| **Overall response rate (CR+PR)** | **1 (33.3)** | **5 (50.0)** | **32 (86.5)** | **7 (58.3)** | **4 (80.0)** | **49 (73.1)** |
| Complete response (CR) | 0 (0) | 4 (40.0) | 16 (43.2) | 5 (41.7) | 2 (40.0) | 27 (40.3) |
| Partial response (PR) | 1 (33.3) | 1 (10.0) | 16 (43.2) | 2 (16.7) | 2 (40.0) | 22 (32.8) |
| Stable disease | 1 (33.3) | 3 (30.0) | 0 (0) | 1 (8.3) | 0 (0) | 5 (7.5) |
| Progressive disease | 0 (0) | 1 (10.0) | 5 (13.5) | 4 (33.3) | 0 (0) | 10 (14.9) |
| Not evaluable | 1 (33.3) | 1 (10.0) | 0 (0) | 0 (0) | 1 (20.0) | 3 (4.5) |

*Best visit response based on 2014 Lugano Criteria

# Swimmers plot




- 77 cHL patients – median 5 prior lines
- 61% refractory to prior line
- 75% prior PD1i
- 45 mcg/kg ORR in cHL: 86.5%; CMR 48.6%

G3+ Aes in 10% or more:

- gammaGT increase
- Maculopapular rash
- Anaemia

Note: 5 pts (all with cHL) developed GBS

Hamadani et al (2021) Lancet haem

# P2 design slide

**Ongoing, Phase 2, single-arm, multicenter, open-label study in patients with R/R cHL[a]**

**30-minute IV infusion of Cami on Day 1 of each 3-week cycle**

**45 µg/kg** → **30 µg/kg**

Cycles 1 & 2

Cycle 3 onwards, up to 1 year[b]

# Phase 2 Baseline characteristics

| Characteristic | | Total (N=117) |
|---|---|---|
| Sex, n (%) | Male | 73 (62.4) |
| | Female | 44 (37.6) |
| Age, years, median (min, max) | | 37 (19, 87) |
| Histology, n (%) | Nodular sclerosis cHL | 91 (77.8) |
| | Other/unknown/not evaluable[a] | 26 (22.2) |
| ECOG status, n (%) | 0 | 63 (53.8) |
| | 1 | 48 (41.0) |
| | 2 | 6 (5.1) |
| No. prior systemic therapies[b], median (range) | | 6 (3–19) |
| Prior BV and PD-1 blockade, n (%) | BV | 116 (99.1) |
| | PD-1 blockade therapy | 117 (100) |
| | BV and PD-1 blockade therapy | 116 (99.1)[c] |
| Prior HSCT, n (%) | Autologous | 58 (49.6) |
| | Allogeneic | 3 (2.6) |
| | Both | 12 (10.3) |
| No. of cycles, mean (SD) | | 4.6 (2.5) |
| Disease status after first-line systemic therapy, n (%) | Relapsed | 77 (65.8) |
| | Refractory | 29 (24.8) |
| | Other[d] | 11 (9.4) |
| Disease status after last-line systemic therapy, n (%) | Relapsed | 38 (32.5) |
| | Refractory | 66 (56.4) |
| | Other[d] | 13 (11.1) |

**At data cut-off (Mar 26, 2021):**

No. of patients enrolled
**117**

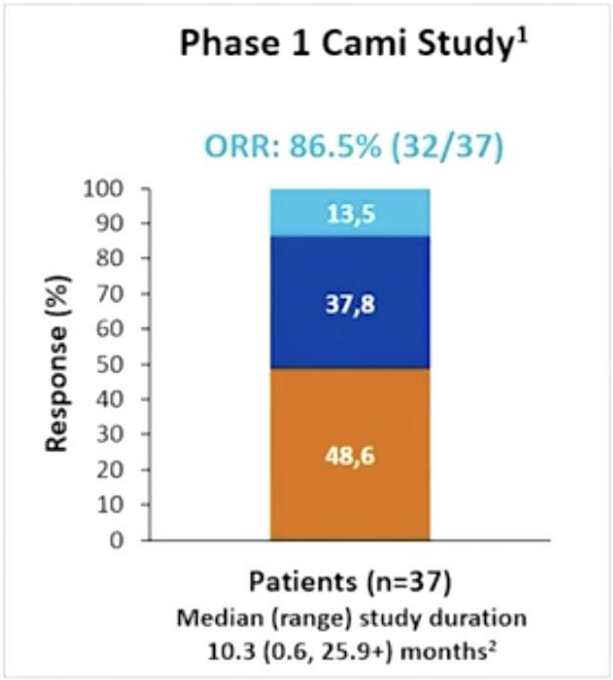
Mean (SD) No. of cycles
**4.6 (2.5)**

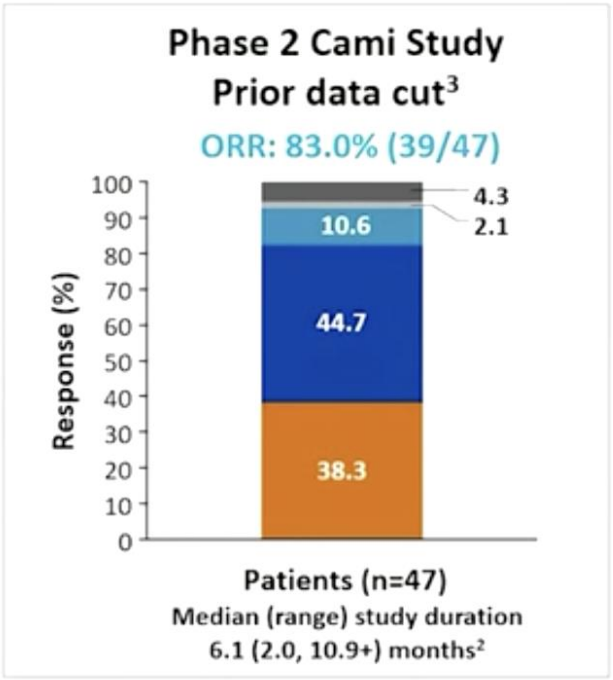
Heavily pre-treated patients; median (range) prior lines of systemic therapy
**6 (3–19)**

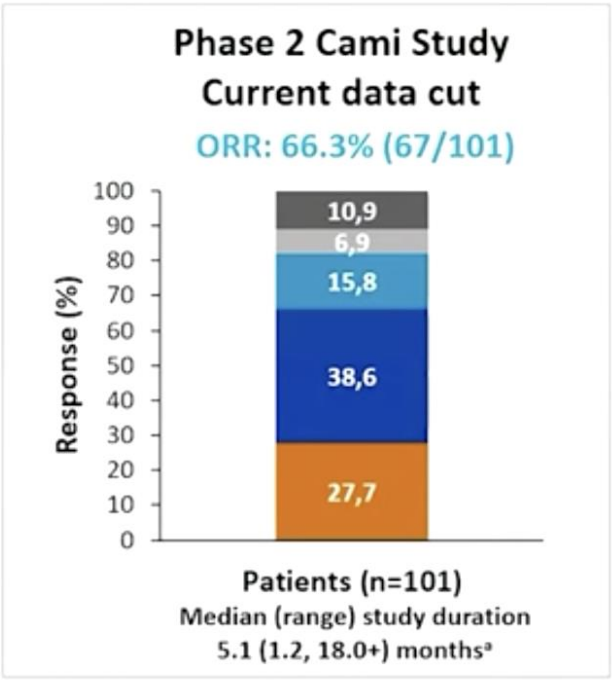
No. of patients with prior brentuximab vedotin and PD-1 blockade therapy
**116 (99.1%)[c]**

Zinzani et al (2021) – ICML oral presentation

# All studies together





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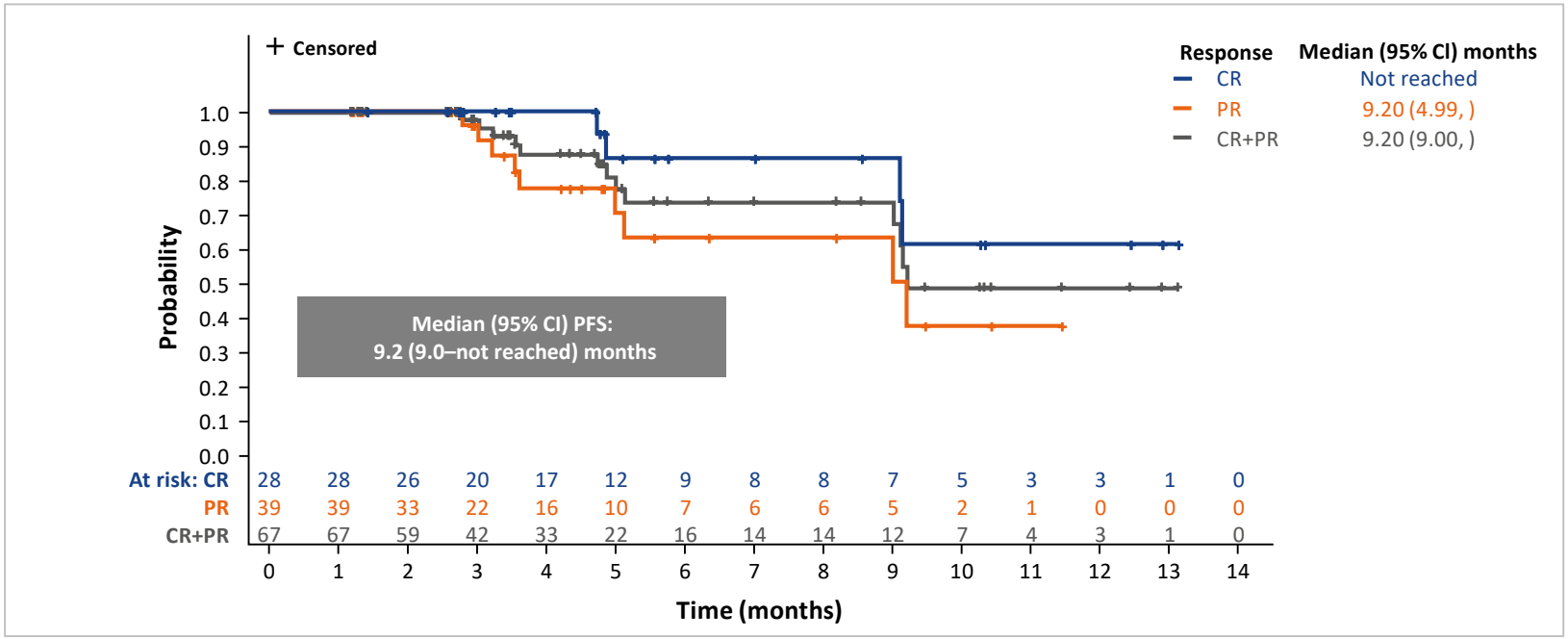
# Progression free survival



# PBD-associated toxicities

## Categories of TEAEs considered PBD-associated

- Skin reactions/nail disorders in 76 (65.0%) patients[a]
- Liver function test abnormalities in 31 (26.5%) patients
- Edema or effusion in 14 (12.0%) patients

## Fatal TEAEs

- Three patients (2.6%) had a fatal TEAE:
  - Myocardial infarction in 1 (0.9%) patient, considered not related to treatment
  - Respiratory failure in 1 (0.9%) patient, considered unlikely related to treatment
  - Adenovirus infection in 1 (0.9%) patient, considered unlikely related to treatment

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# GBS / polyradiculopathy

Total: 7/117 (6.0%) patients. All events were deemed related or probably related to treatment

| AE by preferred term | Study day event start–stop | Max grade | Grade at last assessment | Outcome at last assessment |
|---|---|---|---|---|
| Radiculopathy | Days 41–206 | 2 | - | Recovered/resolved |
| GBS | Days 164–283 | 2 | - | Recovered/resolved |
| GBS | Day 48–ongoing[b] | 3 | 2 | Not recovered/not resolved |
| Polyneuropathy (assessed as polyradiculopathy by Sponsor)[a] | Day 64–ongoing[b] | 3 | 3 | Recovering/resolving |
| GBS | Day 137–ongoing[b] | 3 | 3 | Not recovered/not resolved |
| GBS | Day 24–ongoing[b] | 4 | 3 | Not recovered/not resolved |
| GBS | Day 101–ongoing[b] | 4 | 4 | Not recovered/not resolved |

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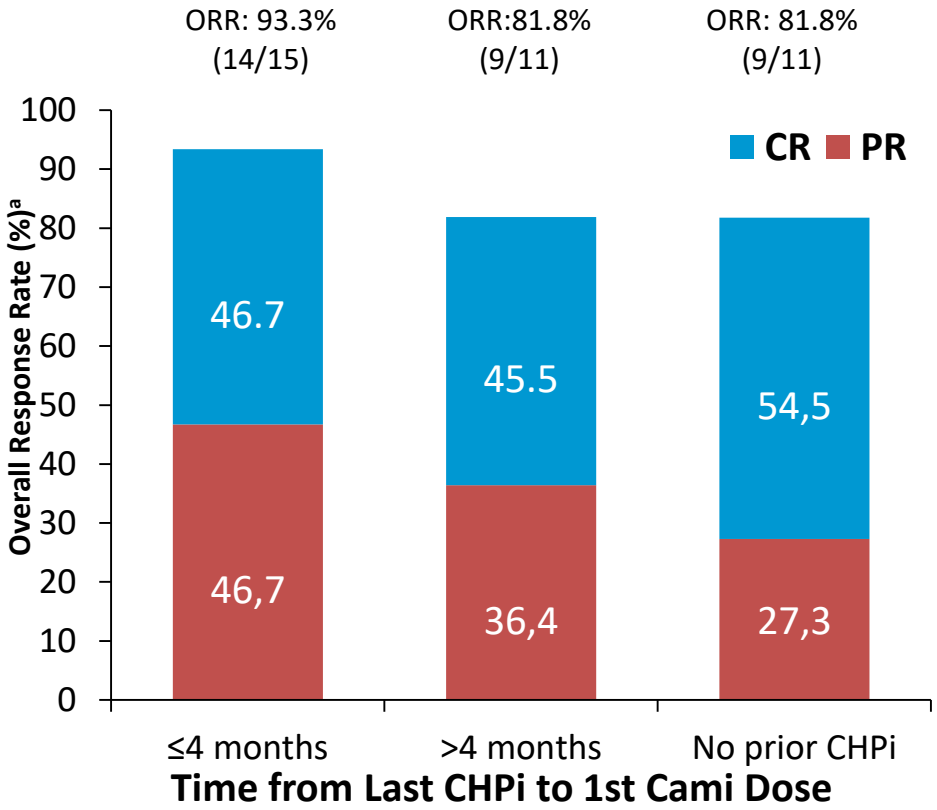
# GBS and anti-CD25 targeting

- Regulatory T-cells are implicated in the pathogenesis of GBS: low levels in blood of GBS patients[1]; IVIG associated with increased Treg[2]
- BUT only patients with Hodgkin treated with Cami-T have developed GBS / polyradiculopathy
- Other anti-CD25 agents are NOT associated with significant rates of GBS e.g. daclizumab[3]
- Other CD25 targeting agents in Hodgkin have not been associated with GBS e.g. 90Y-anti-CD25[4,5]
- Appears to be specifically more common in Hodgkin and cami-T treated patients

[1]Harness and Mccombe (2008) J Clin Neurosci
[2]Zhang et al (2019) J Neuroimmunology
[3]Kappos et al (2021) Ther Adv Neurol Disorders
[4]Janik et al (2015) PNAS
[5]Herrera et al (2021) Blood Adv

# Relationship to prior PD1i (phase 1 data)




| Selected TEAE groups, n (%)[b] | 45 µg/kg cohort (N=37) | | |
|---|---|---|---|
| | ≤ 4 months (N=15) | > 4 months (N=11) | None (N=11) |
| Edema or effusion | 5 (33.3) | 2 (18.2) | 3 (27.3) |
| Liver function test | 6 (40.0) | 4 (36.4) | 3 (27.3) |
| Skin related | 10 (66.7) | 8 (72.7) | 7 (63.6) |
| Autoimmune | 5 (33.3) | 4 (36.4) | 2 (18.2) |
| Neurologic | 4 (26.7) | 3 (27.3) | 3 (27.3) |
| Guillain-Barre syndrome/radiculopathy* | 1 (6.7) | 1 (9.1) | 1 (9.1) |

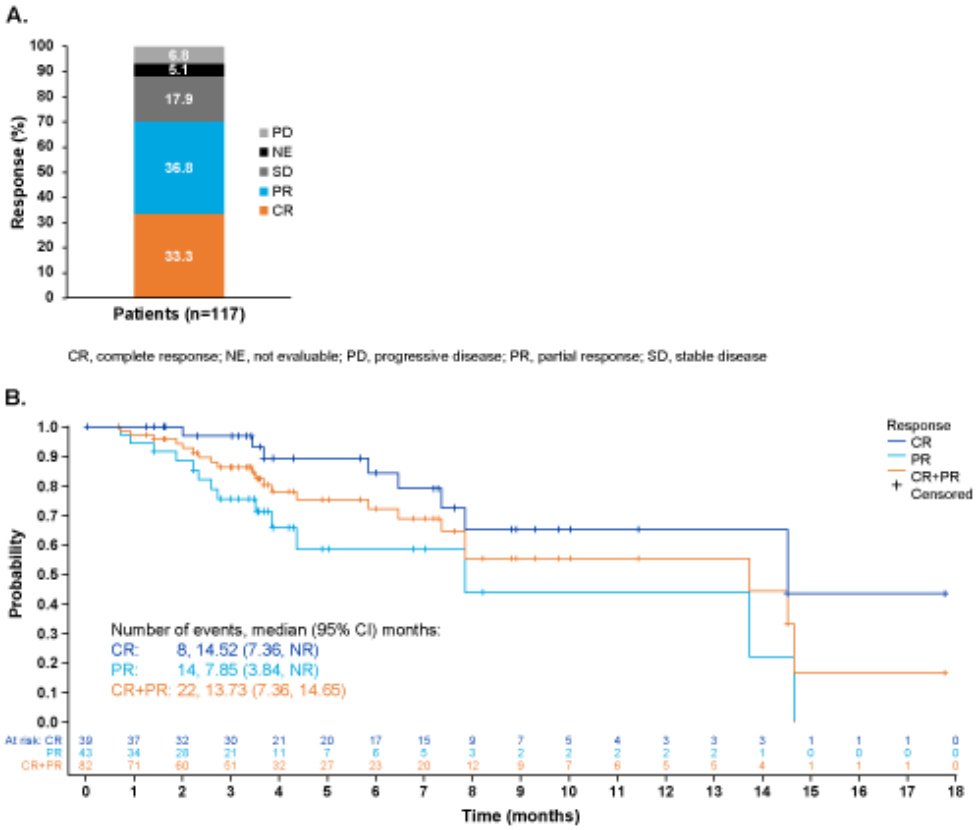
*2 other events occurred at 30 and 60 µg/kg doses in the >4 months and none groups, respectively

Collins *et al* (2019) – ICML oral presentation

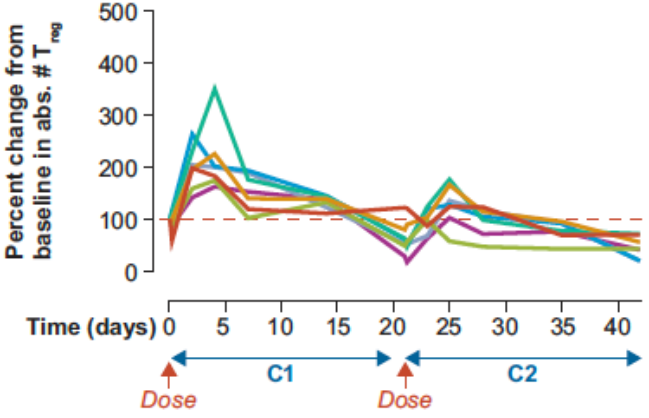
# EHA 2022 update

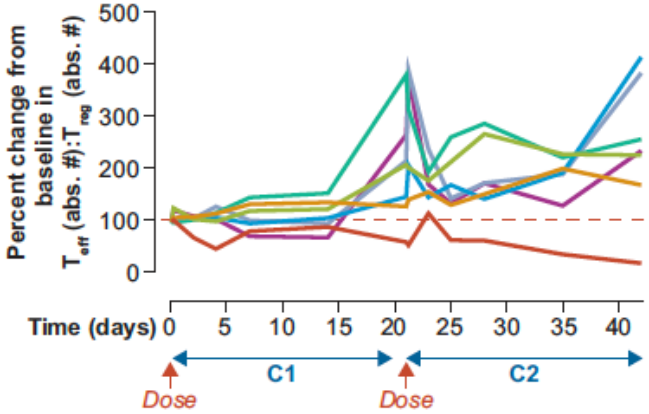
Data being presented at EHA22, Carlo-Stella et al

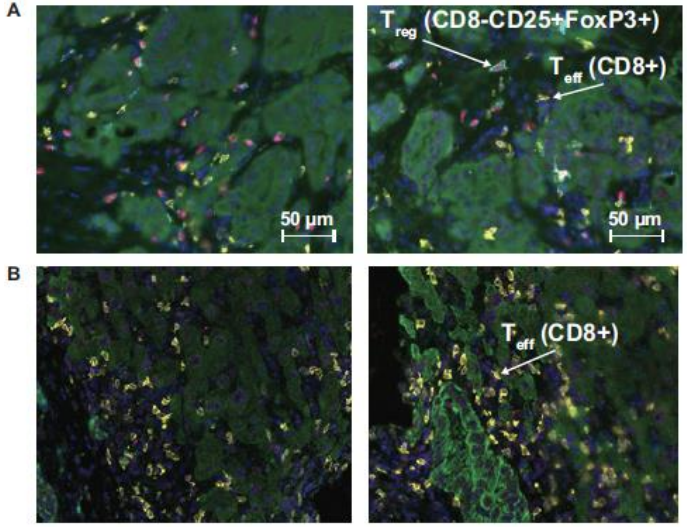
- ORR 70.1%; CRR 33.3%
- Median FU 10.7mo
- Median DOR 13.7mo (14.5mo for CR)
- Median PFS 9.1mo
- GBS / polyradiculopathy in 6.8%

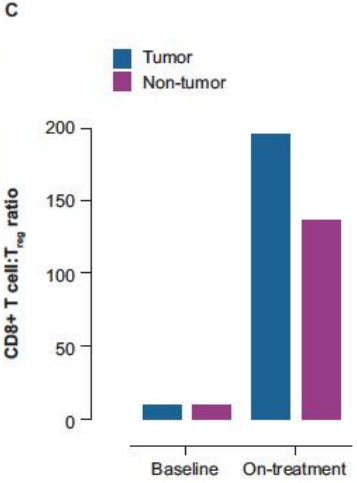


# Changes in lymphocyte populations




Puzanov et al (2020) ESMO

- Cami-T in solid tumour patients
- Gradual reduction in Treg population in peripheral blood
- Gradual rise in Teff:Treg ratio
- In paired tumour samples, about 50% showed increased Teff:Treg
- Saw increased PB Teff:Treg ratio in Hodgkin patients on the Ph1

# Conclusions

- Cami-T is a CD25 targeting agent tested in P1 and P2 trials in Hodgkin lymphoma
- High response rates in heavily pretreated patients are seen
- Significant toxicities are seen:
  - PBD related: skin, liver, effusions
  - Immunological: GBS, thyroid disturbance
- GBS not only the result of Cami targeting CD25
- No details yet on randomized study to support license application

# Acknowledgements


- Patients, their carers and families for supporting trials
- All the PIs and trial teams involved in the Cami studies

# Thank you for listening

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Oxford University Hospitals NHS
NHS Foundation Trust

**Oxford Lymphoid Disorders Study Group**

Uniting Researchers, Fighting Lymphoid Cancers