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UChicago
Medicine

ASH 2022

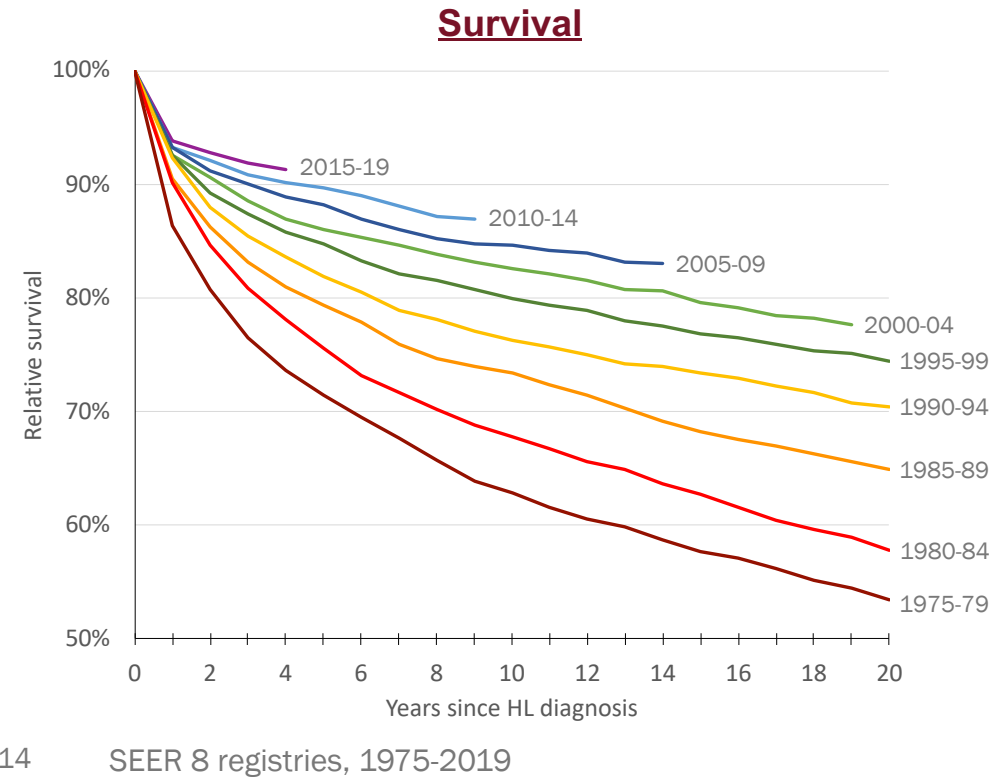
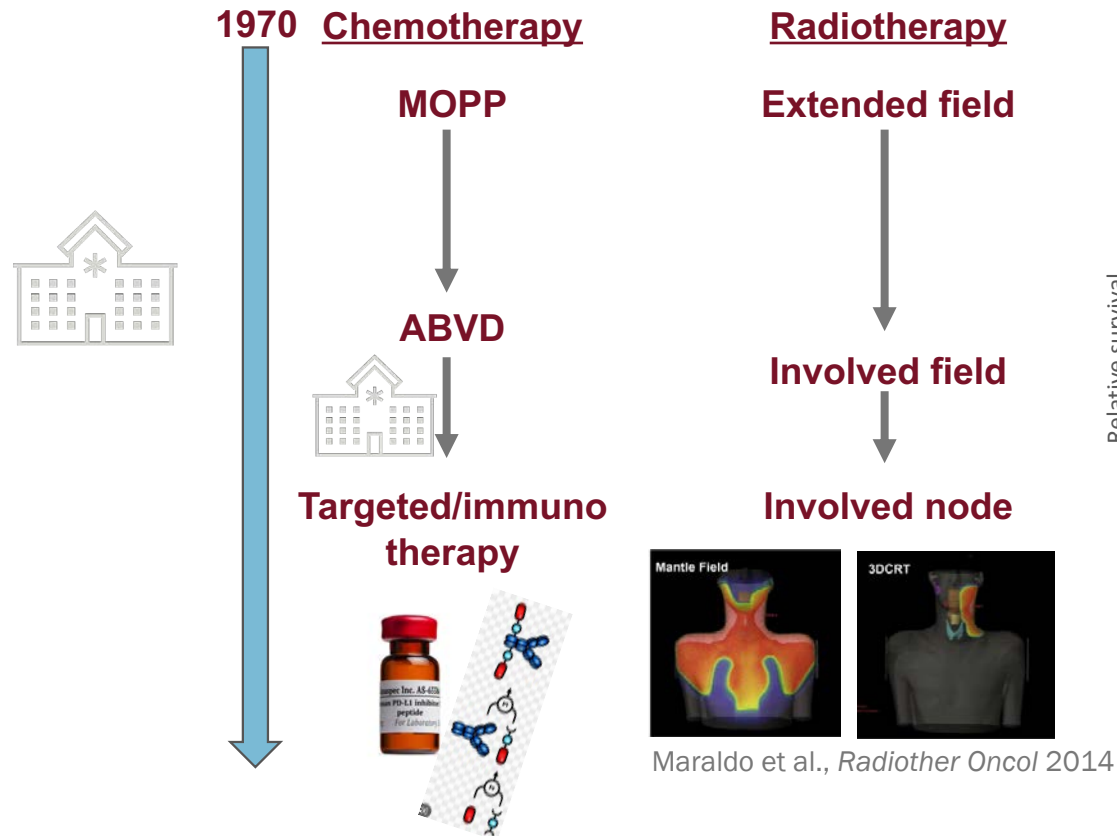
HODGKIN LYMPHOMA

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Co-Leader, Cancer Service Line
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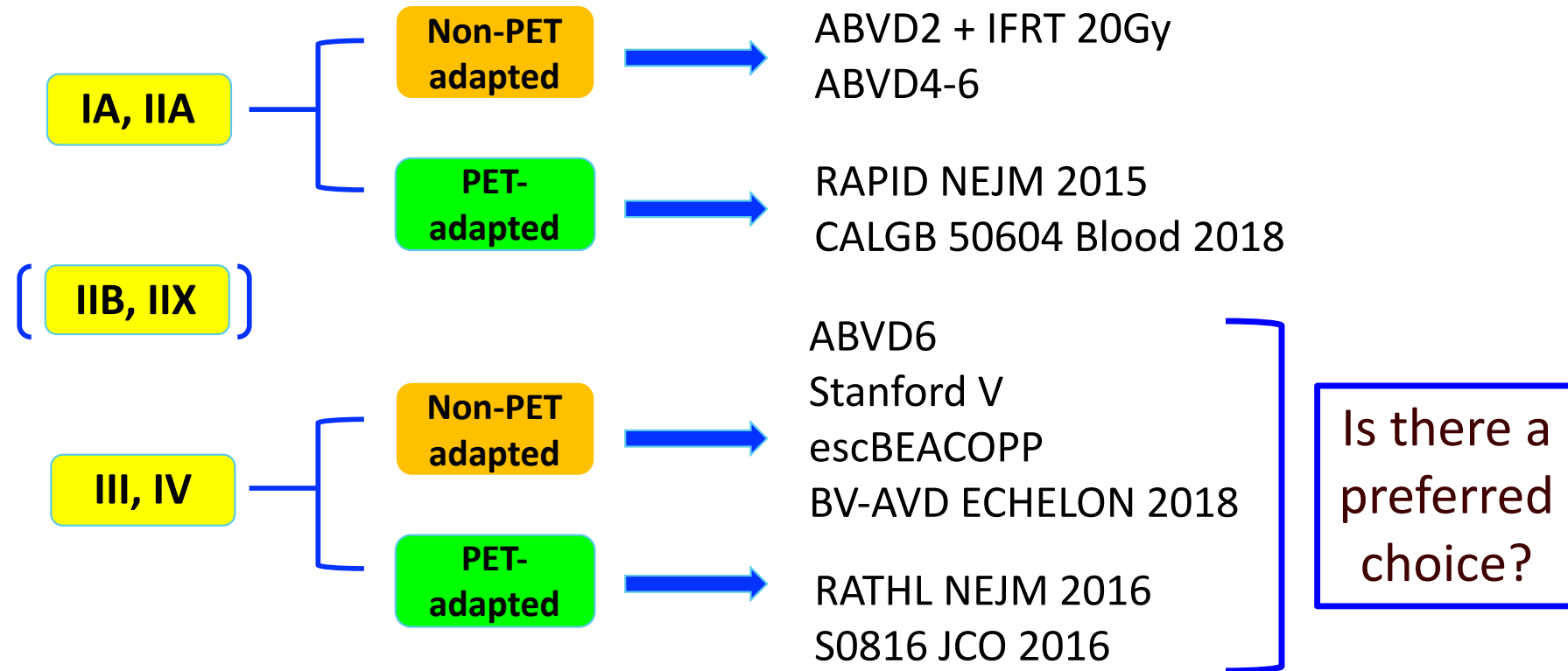
Hodgkin Lymphoma

- Long-term follow-up from the Phase III ECHELON-1 trial of first-line brentuximab vedotin (BV) with AVD for advanced classical HL
- Early findings with BV-based therapy for early-stage, unfavorable-risk HL
- Available data with BV for older patients with newly diagnosed advanced HL
- Mechanism of action of and available efficacy and safety findings with camidanlumab tesirine for patients with R/R HL
- Other promising investigational strategies for patients with HL (eg, novel immunotherapeutic strategies, CAR T-cell therapy)

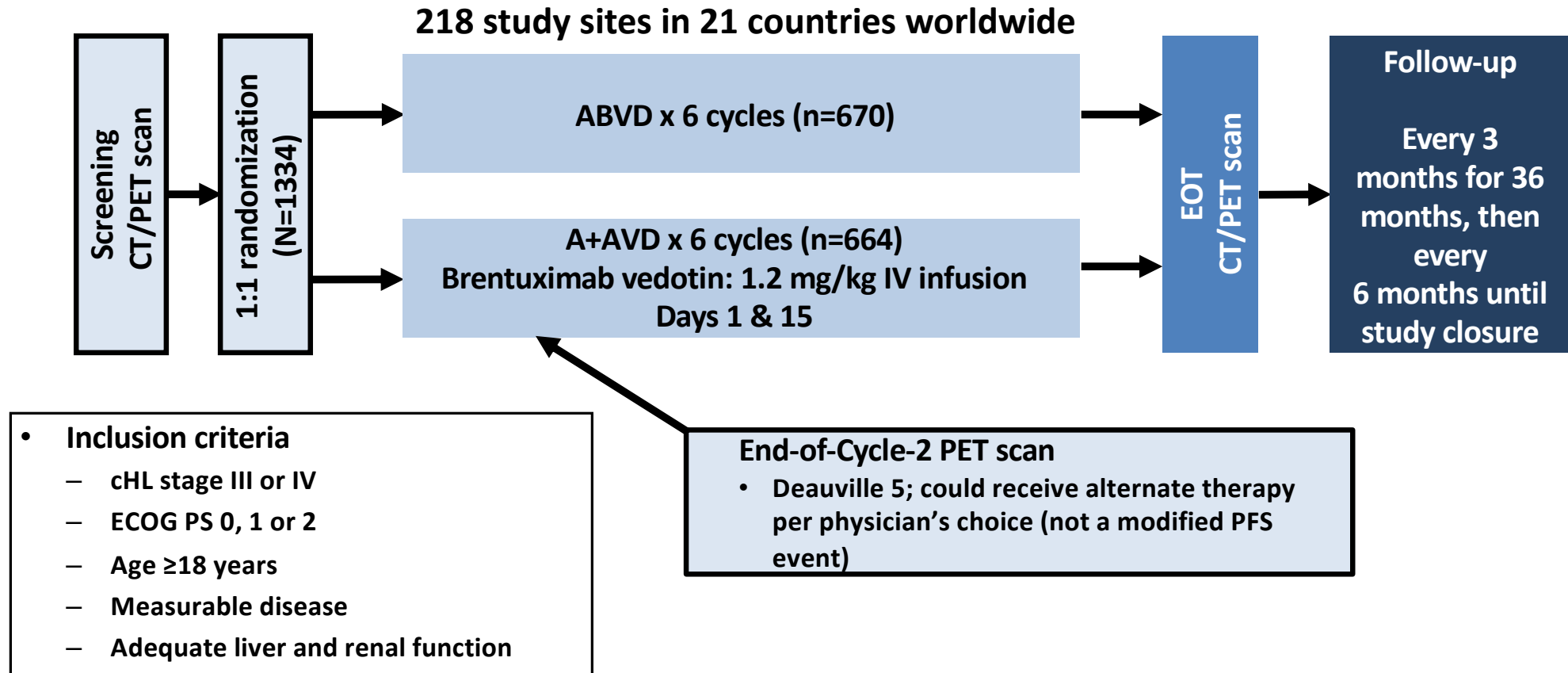
Evolution of Hodgkin Lymphoma Treatment



Hodgkin lymphoma: frontline standard treatment approach can be PET-adapted or non PET-adapted



ECHELON-1: BV-AVD vs. ABVD (not PET-adapted)

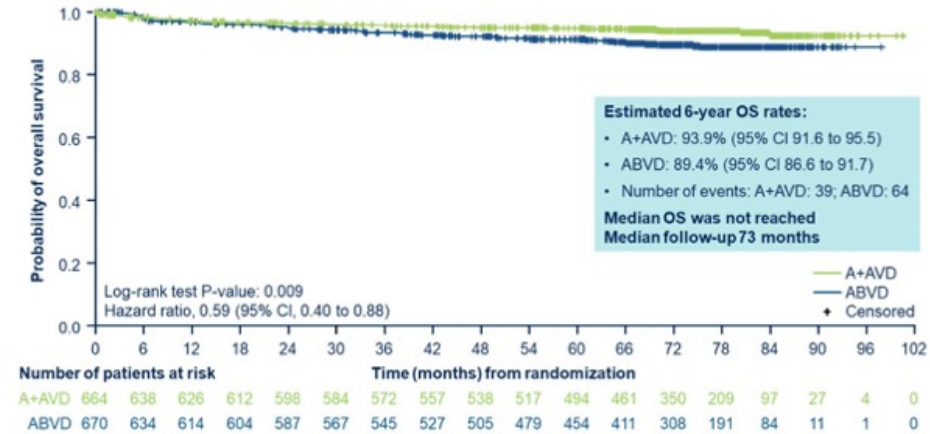


ECHELON-1 results (73m median f/u)

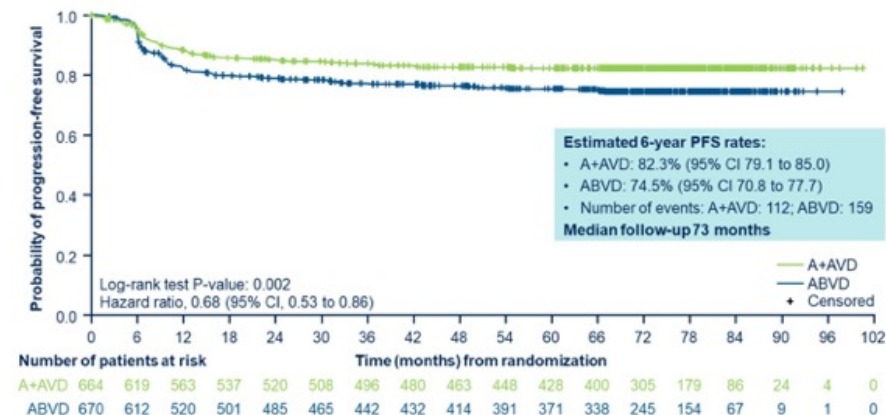
BV-AVD arm

- Fewer disease- or treatment-related progression and deaths
- Fewer second malignancies and fewer deaths due to second malignancies
- More reported pregnancies (113 vs. 78)
- 86% of pts had resolution of peripheral neuropathy symptoms

A+AVD significantly improved OS with a 41% reduction in risk of death compared with ABVD

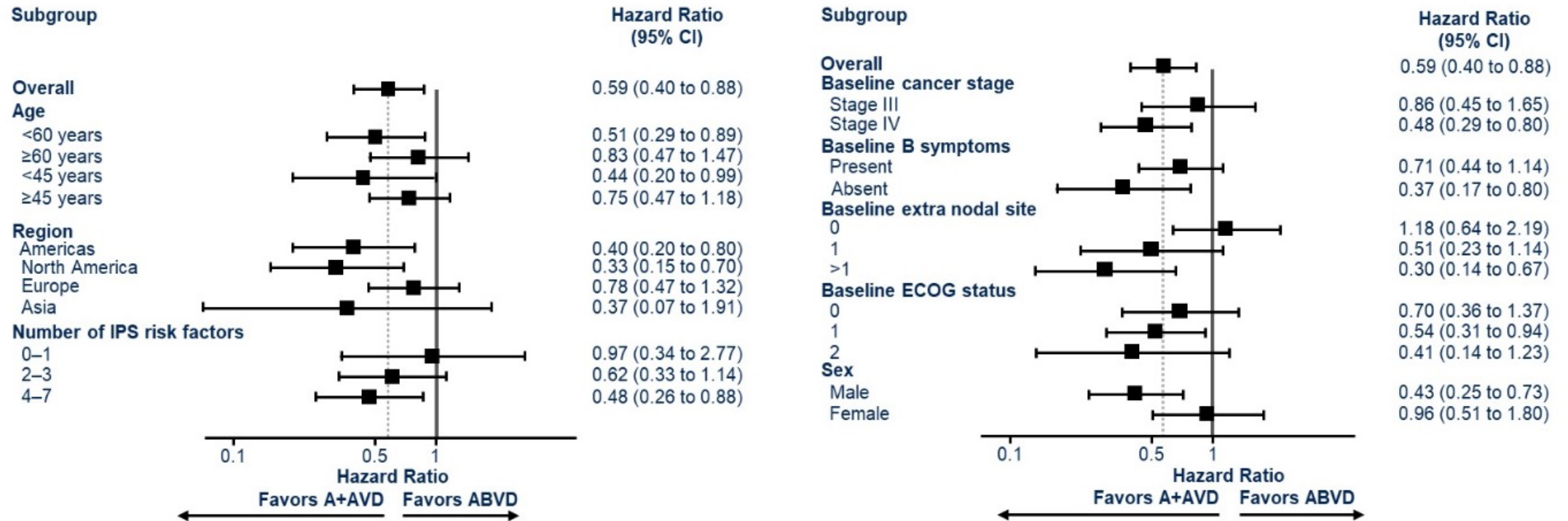


A+AVD reduced the risk of progression or death by 32% when compared with ABVD



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OS benefit across subgroups

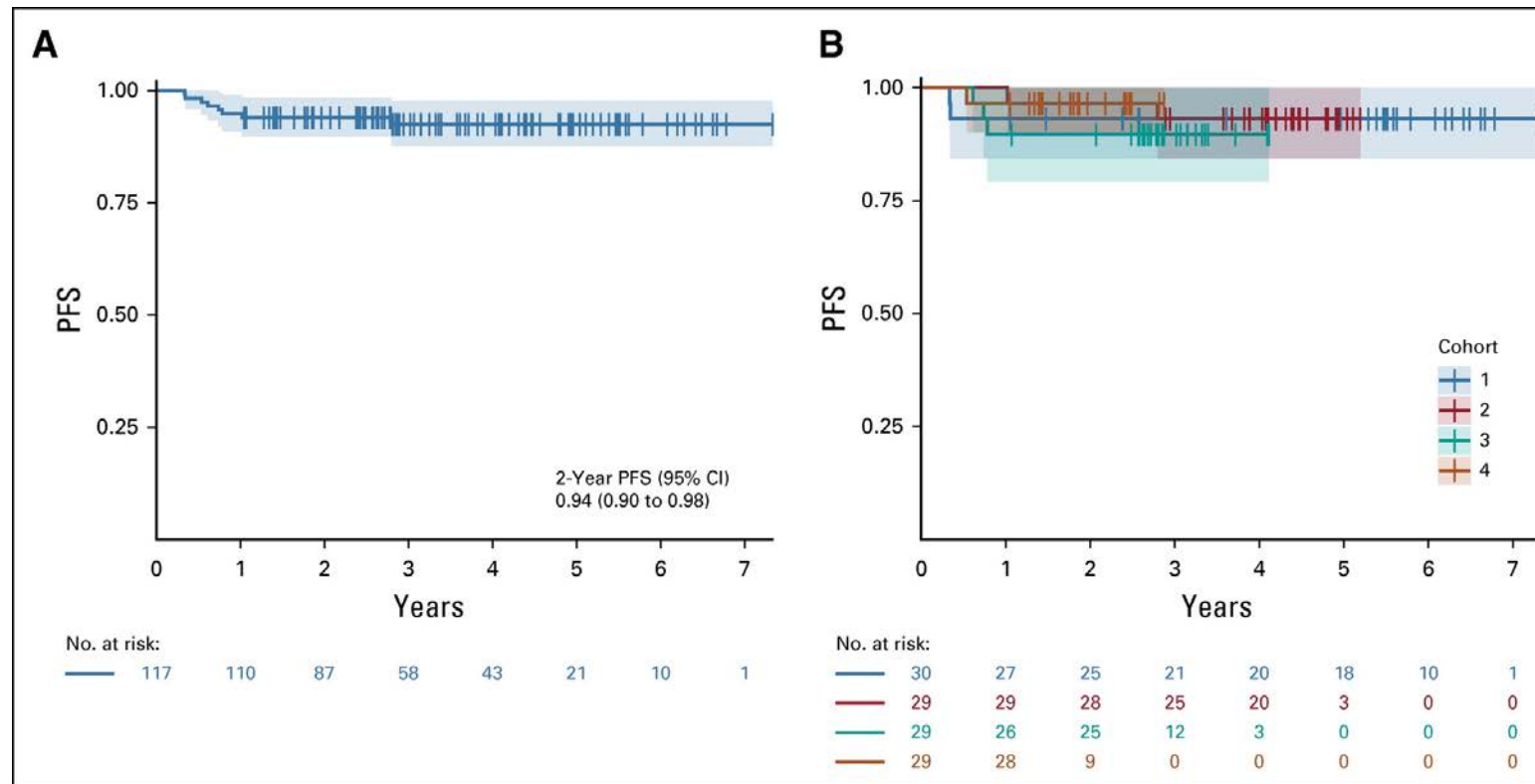


- The OS benefit with A+AVD was preserved in a multivariable analysis when simultaneously adjusting for baseline demographic and disease factors (HR 0.53; 95% CI, 0.34 to 0.83)
 - Age, non-white race, ECOG performance status score, and PET2 status were identified as the covariates with greatest evidence of association with overall survival

BV-based regimens in limited stage cHL

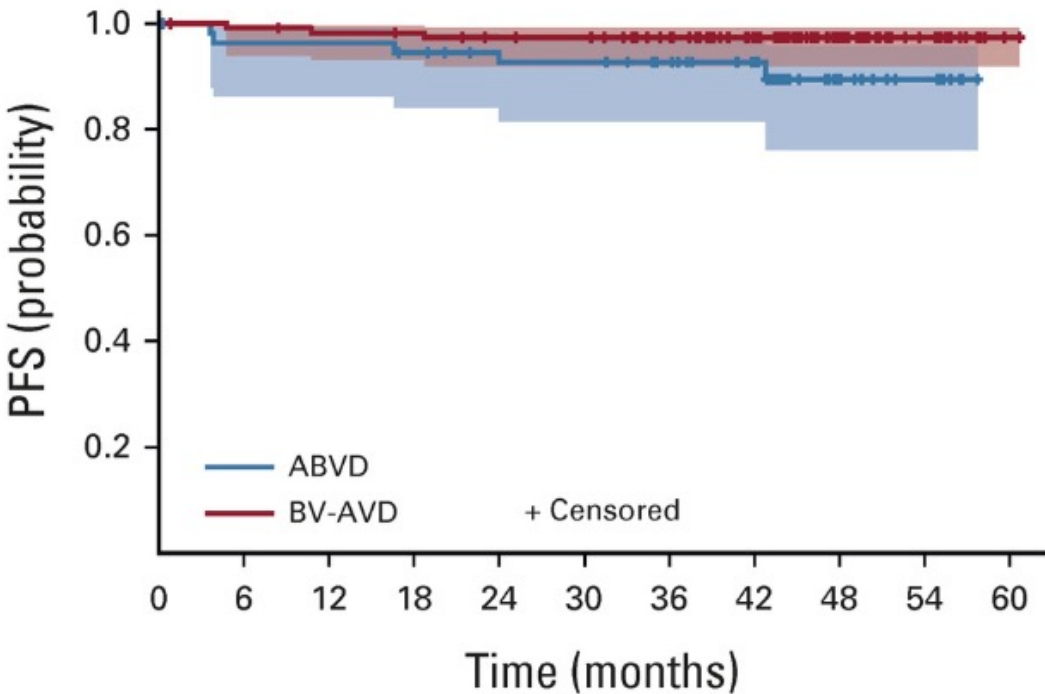
Early stage cHL with
unfavorable features
(including bulky disease)

BV-AVD x 4 → if PET neg → 3 RT cohorts
1 no RT cohort



N=117

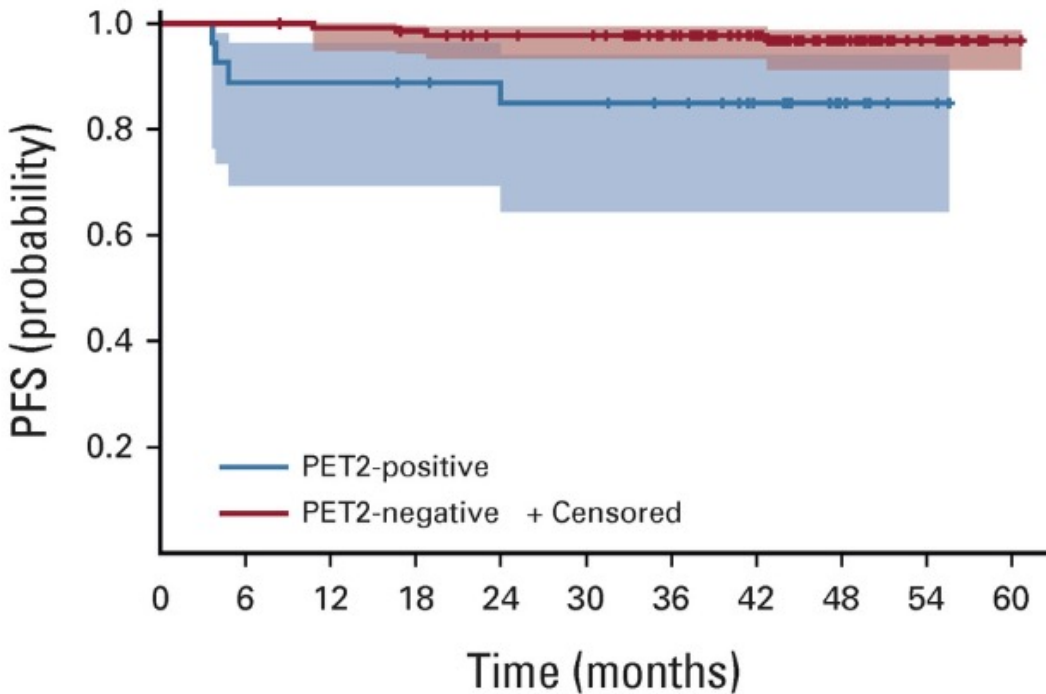
RP2 trial of BV-AVD v. ABVD (2:1) in limited stage unfavorable cHL (LYSA-FIL-EORTC Intergroup): BREACH trial



No. at risk:

ABVD	57	53	53	51	47	47	42	33	15	7	0
BV-AVD	113	111	109	108	105	104	97	80	44	17	2

PFS by treatment arm



No. at risk:

PET2-positive	27	24	24	23	21	21	19	14	7	2	0
PET2-negative	136	136	134	132	127	126	116	95	50	21	1

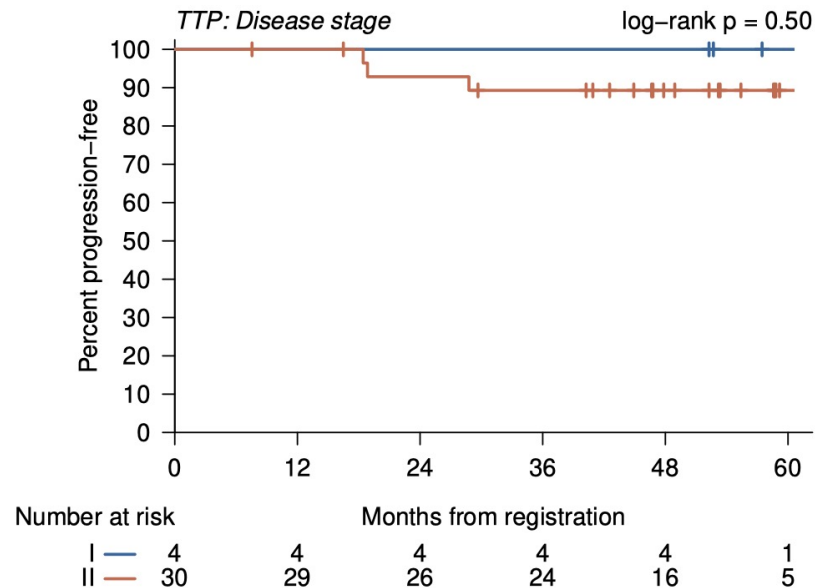
PFS by PET2 status

If BV is used, can vinblastine be omitted? Can nivo be added?

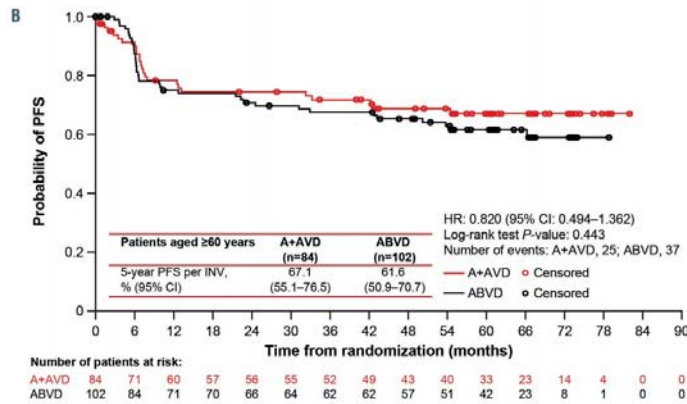
BV plus AD x 4-6 cycles (N=34)
PET-adapted phase 2 trial
non-bulky, limited st dz
Med f/u 53m

BV plus nivo plus AD (AN-AD) x 4
non-bulky, limited st dz
(abstract 4230)

BV-AVD x 3 → Nivo consol.
non-bulky, limited st dz
(abstract 728)

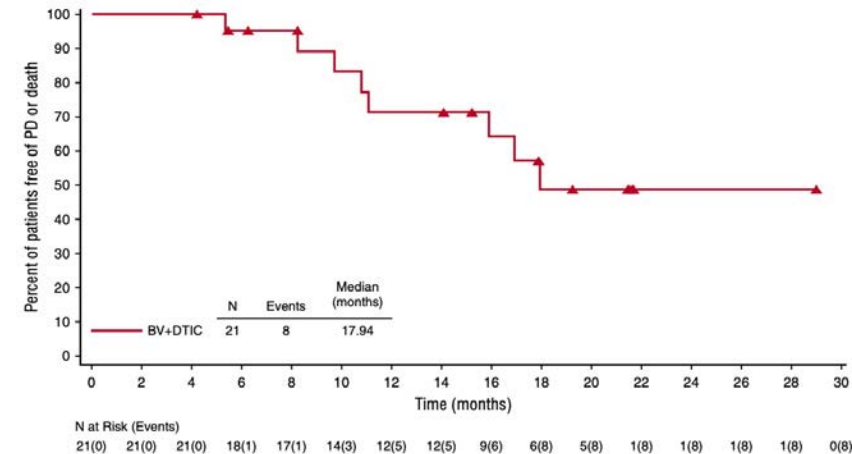


Treatment of older patients with cHL

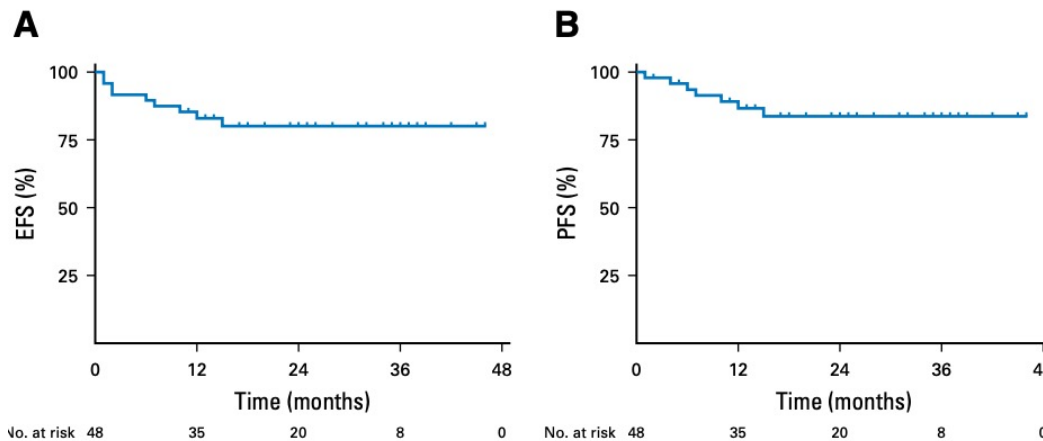


ECHELON-1: BV-AVD = ABVD

(more neuropathy and neutropenia but less pulmonary toxicity than ABVD)



BV plus DTIC



Other:

- RATHL approach (only 10% ≥ 60y)
- AVD
- CHOP

BV → AVD → BV

Camidanlumab tesirine: anti-CD25 plus PBD dimer ADC

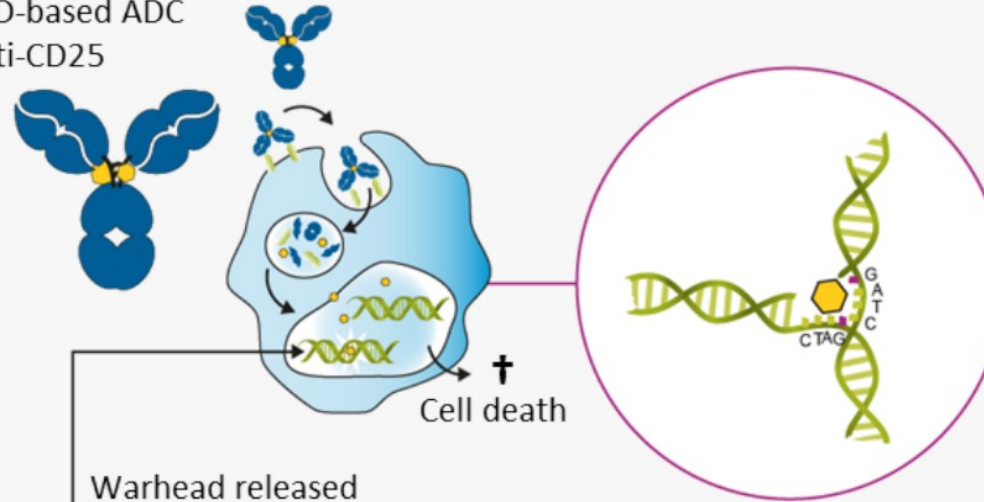
Cami composition

- Human IgG1 anti-CD25 mAb stochastically conjugated to PBD dimer warhead

Mechanism of action¹⁻³

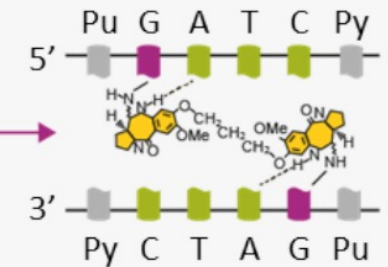
- Death of CD25-expressing tumor cells
- Depletion of CD25-expressing T cells in HL tumor microenvironment
- Possible bystander killing of CD25-negative cells

PBD-based ADC
Anti-CD25



Warhead released after internalization and binds in minor groove of DNA

Cross-link DNA



- PBD dimer creates interstrand cross-links
- No DNA distortion
- Avoids DNA repair mechanism

1. Hartley JA. *Expert Opin Investig Drugs* 2011;20:733–44; 2. Flynn MJ, et al. *Mol Cancer Ther* 2016;15:2709–21; 3. Zammarchi F, et al. *J ImmunoTher Cancer* 2020;8:e000860.

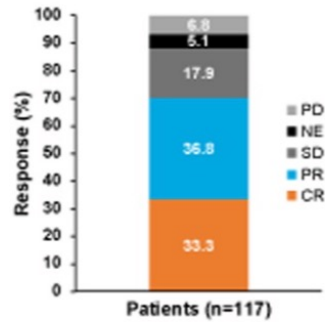
ADC, antibody-drug conjugate; IgG, immunoglobulin G; mAb, monoclonal antibody; PBD, pyrrolobenzodiazepine.



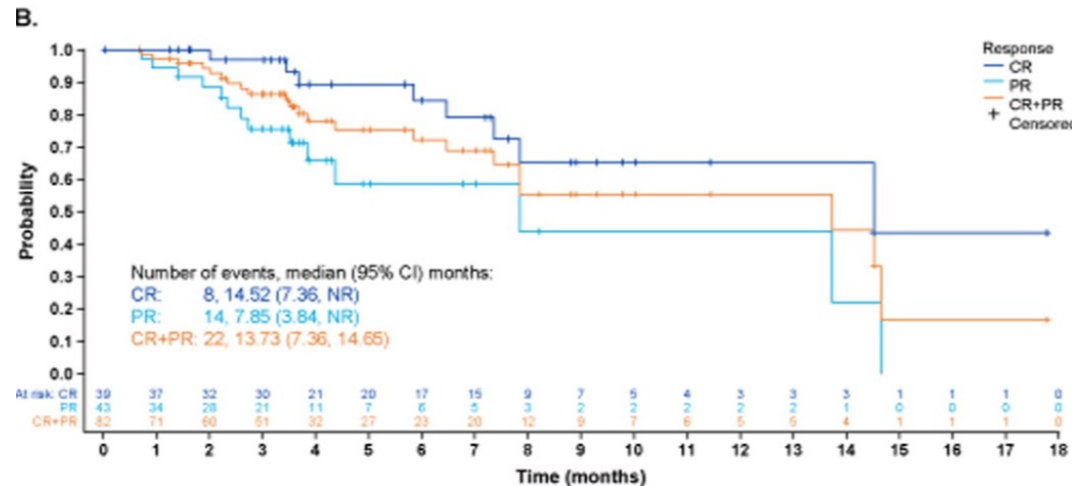
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Ph 2 International monotherapy trial of cami (NCT04052997)



CR, complete response; NE, not evaluable; PD, progressive disease; PR, partial response; SD, stable disease



Key findings:

N=117 with med SIX prior regimens

ORR 70.1% (CR: 33.3%)

Response independent of age, sex,
response to last PD-1 inhibitor

Median DOR of 13.7m

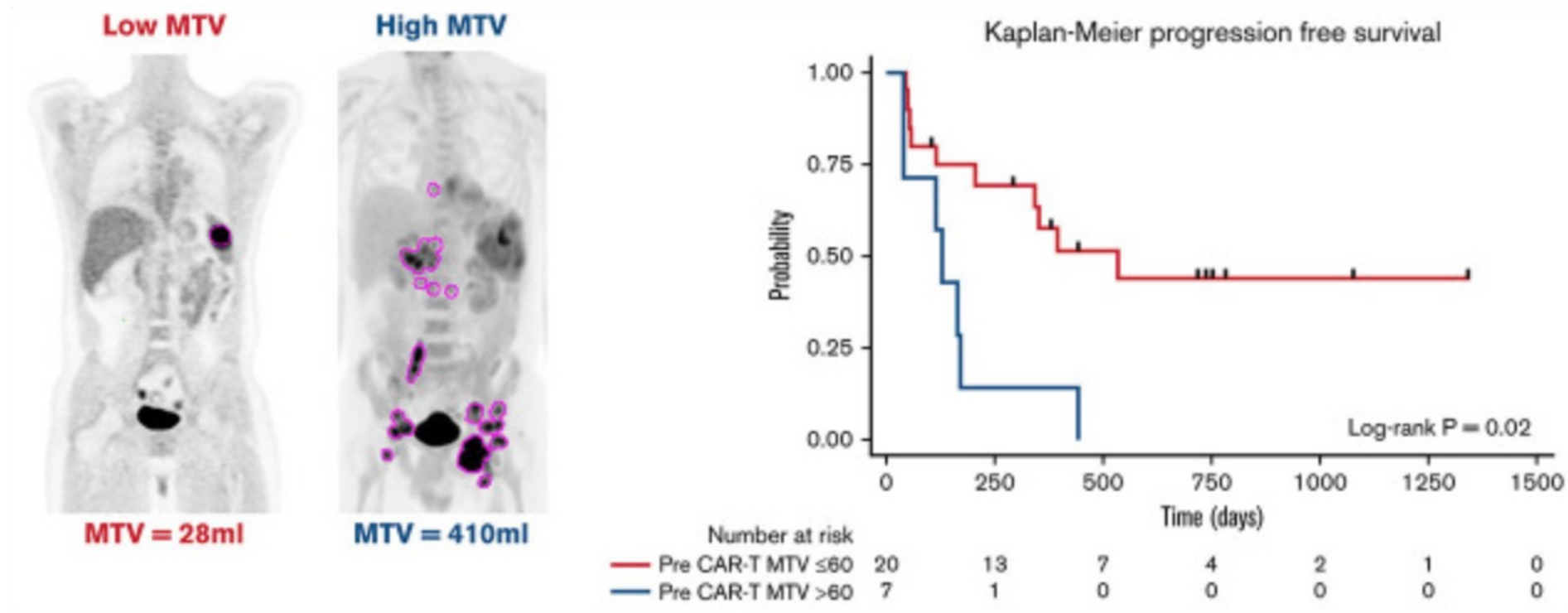
Median PFS of 9.1m

Guillan-Barre syndrome in 8 pts



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Emerging therapies: anti-CD30 CAR-T

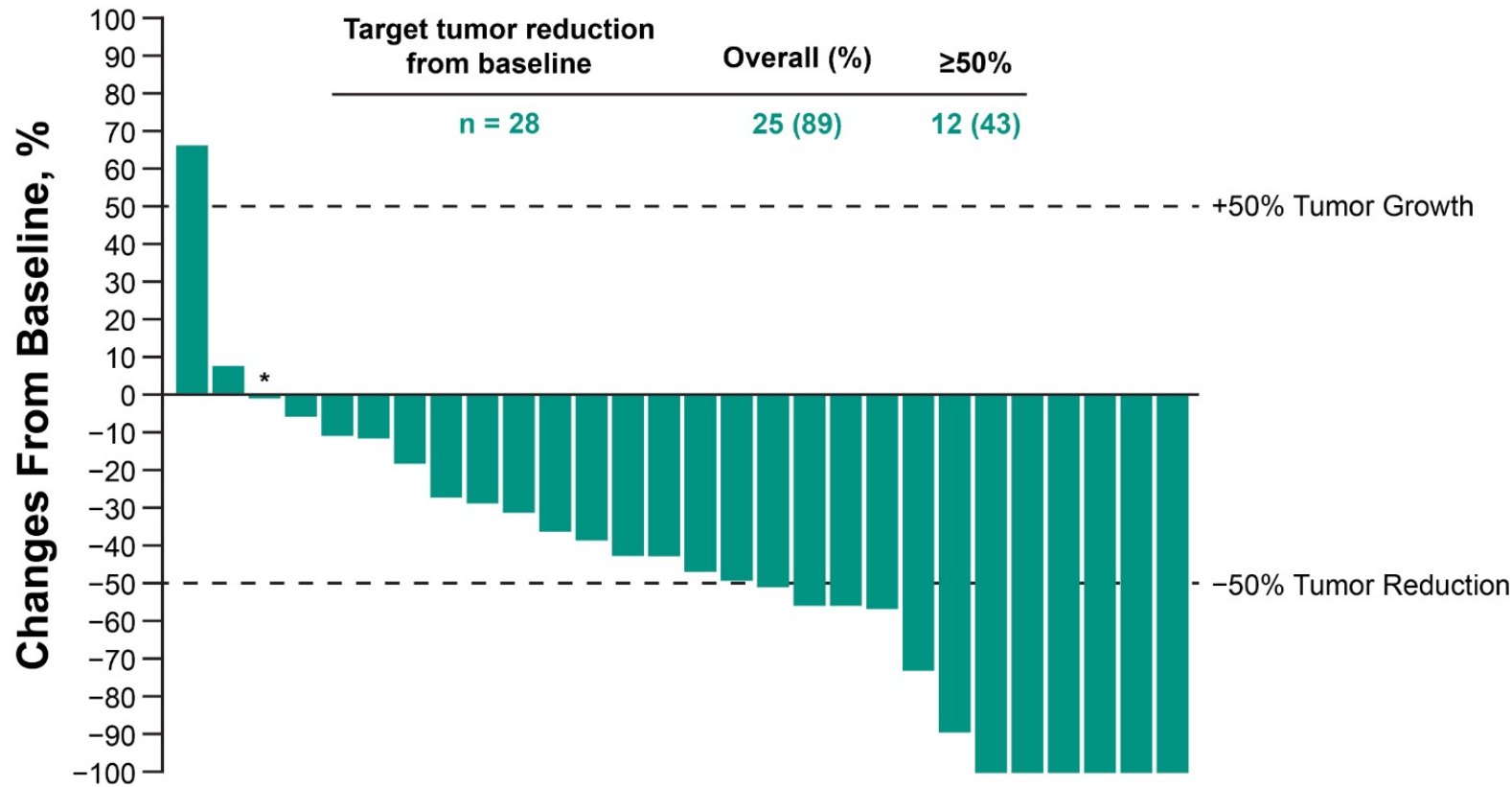


CAR-T outcomes in cHL by pre-CAR-T MTV (n=27)

Emerging CAR-T for cHL: “off the shelf”

ASH 2022 Abstract 167 CD30.CAR-Modified Epstein-Barr Virus-Specific T Cells (CD30.CAR EBVSTs) Provide a Safe and Effective Off-the-Shelf Therapy for Patients with CD30-Positive Lymphoma

Next steps for immunotherapy in cHL? Dual blockade of LAG-3 and PD-1



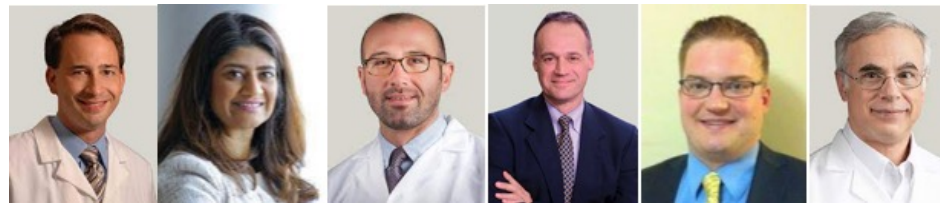
*Value is +0.16

ASH 2022 abstract 316 Updated Results from an Open-Label Phase 1/2 Study of Favezelimab (anti-LAG-3) Plus Pembrolizumab in Relapsed or Refractory Classical Hodgkin Lymphoma after Anti-PD-1 Treatment (Timmerman)



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THANK YOU!!



LYMPHOMA PROGRAM:
The University of Chicago
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APPENDIX

Hodgkin Lymphoma (HL) — Dr Smith

Total Slides: 16

Data Slides: 13

- Long-term follow-up from the Phase III ECHELON-1 trial of first-line brentuximab vedotin (BV) with AVD for advanced classical HL
 - Slides 5-7
- Early findings with BV-based therapy for early-stage, unfavorable-risk HL
 - Slides 8-10
- Available data with BV for older patients with newly diagnosed advanced HL
 - Slide 11
- Mechanism of action of and available efficacy and safety findings with camidanlumab tesirine for patients with R/R HL
 - Slides 12-13
- Other promising investigational strategies for patients with HL (eg, novel immunotherapeutic strategies)
 - Slides 14-16