# Is there a role for Brentuximab vedotin in Diffuse Large cell Lymphoma?

Stephen M. Ansell, MD, PhD
Professor of Medicine
Mayo Clinic

# Disclosures for Stephen Ansell, MD, PhD

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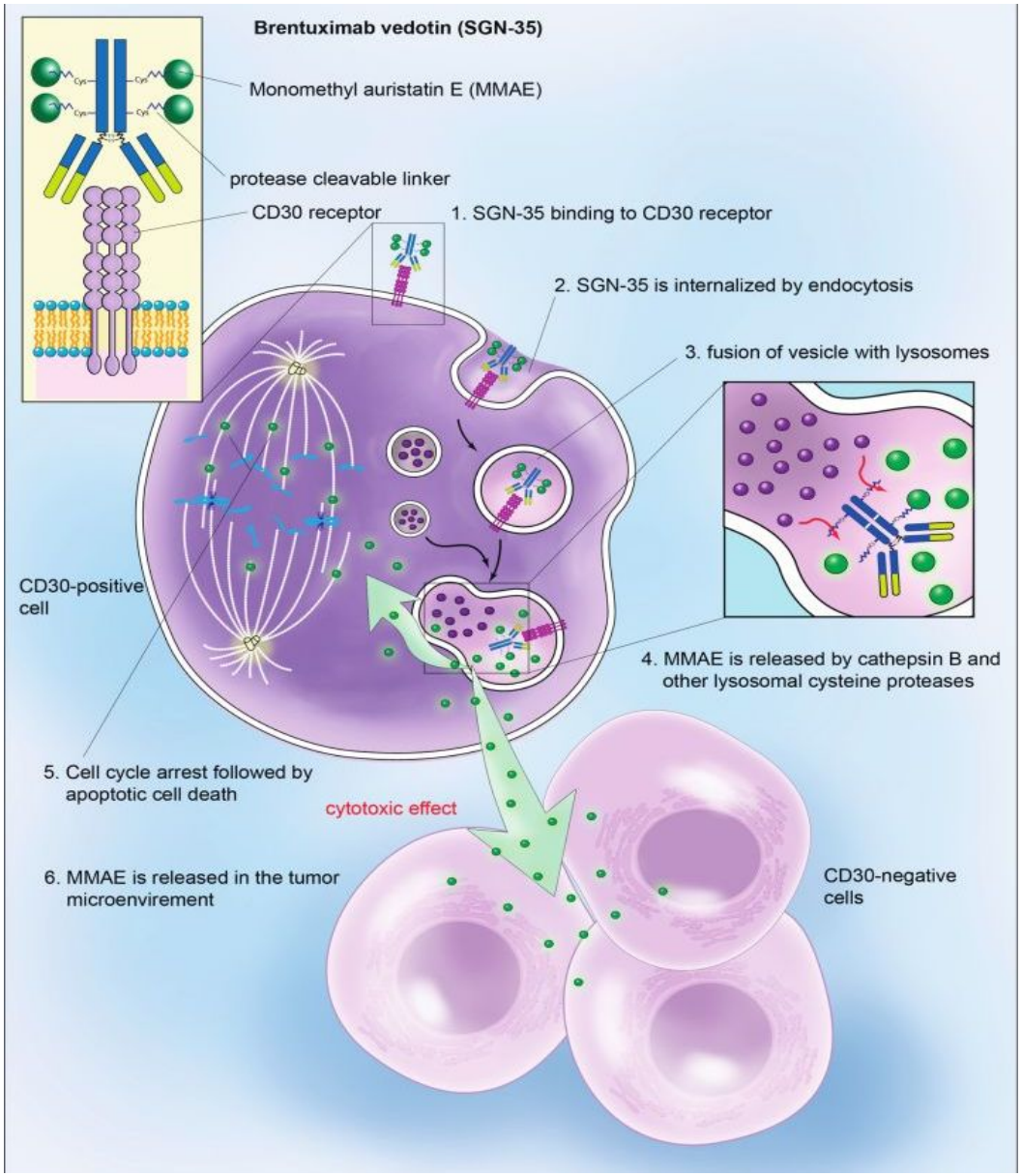
| | |
|---|---|
| Research Support/P.I. | PI – Seattle Genetics, Bristol Myers Squibb, Celldex |
| Employee | N/A |
| Consultant | N/A |
| Major Stockholder | N/A |
| Speakers' Bureau | N/A |
| Scientific Advisory Board | N/A |

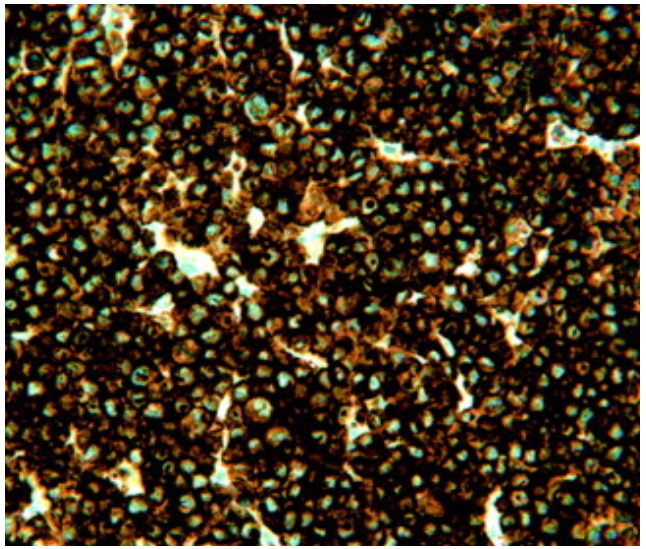
**N/A = Not Applicable (no conflicts listed)**

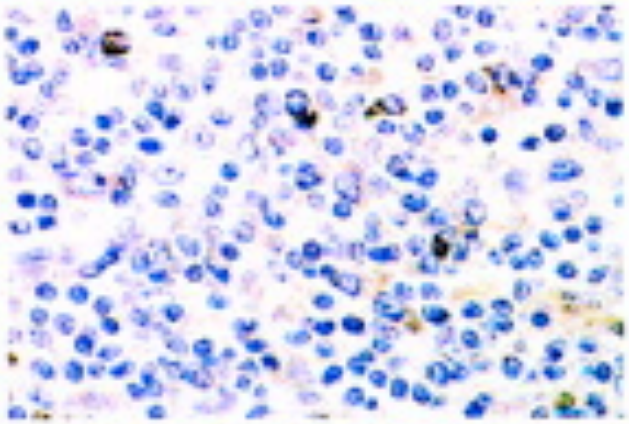
# Brentuximab vedotin in DLBCL

- Why would we expect it to add anything?
- What is the single agent activity with BV?
- What are the results in combination with other agents?
- What's its role in DLBCL?

# Brentuximab vedotin – Mechanisms of action

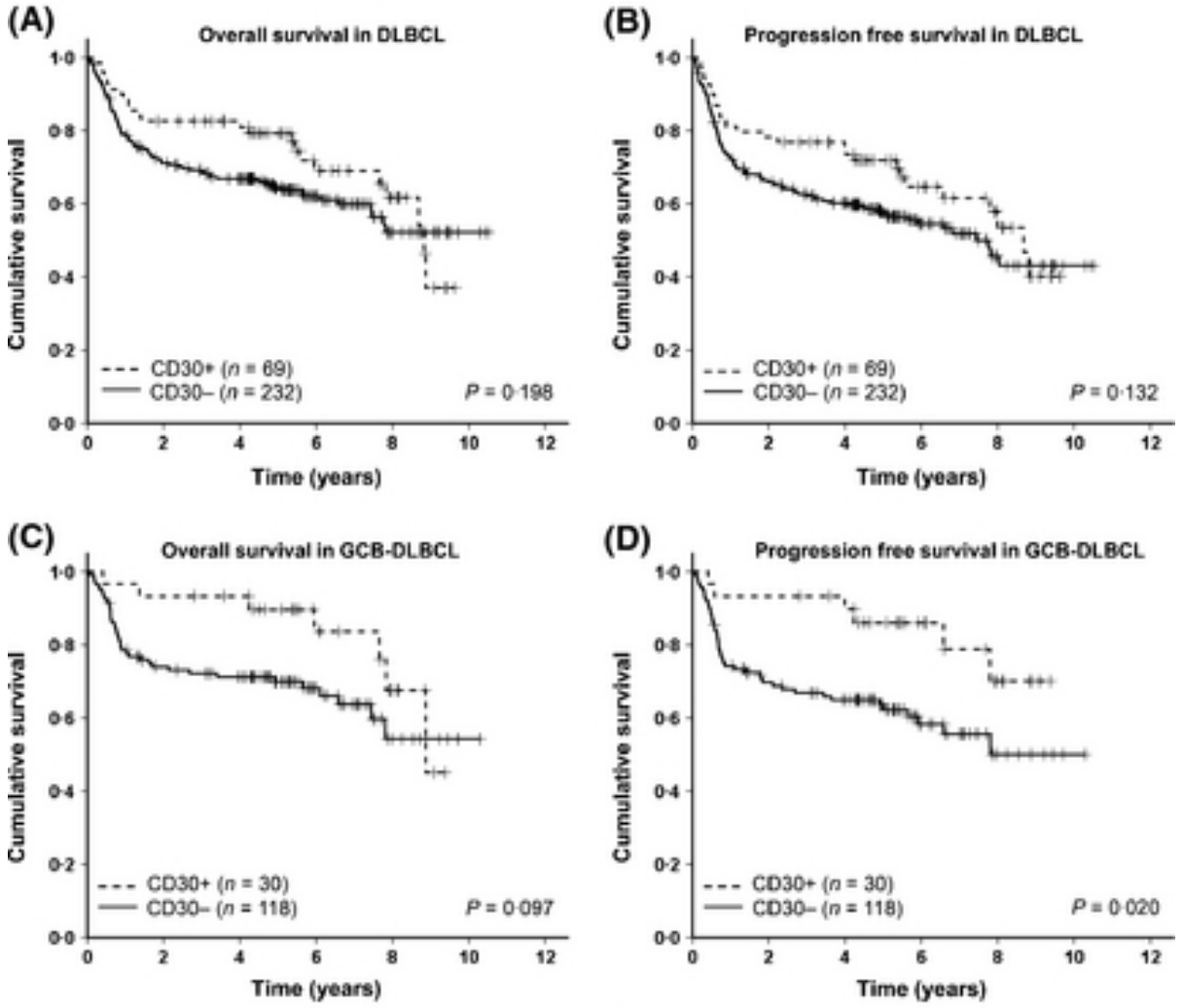




Vaklavas et al. Ther Adv Hem. 2012;3(4):209-225.
Brown et al. Immunotherapy. 2014 Apr;6(4):371-5.

# CD30 expression in *de novo* diffuse large B-cell lymphoma



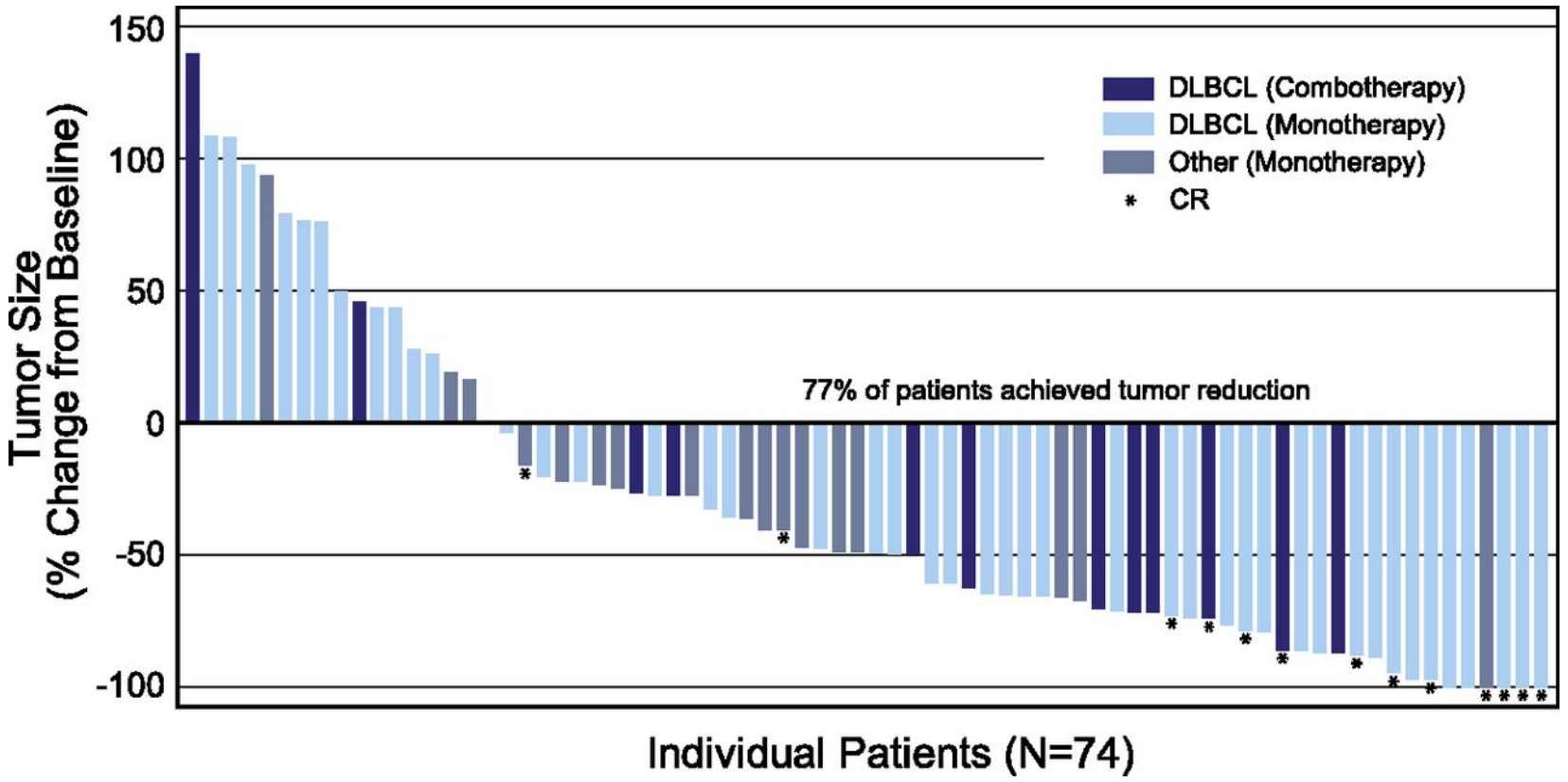

Slack et al. Br J Haematol. 2014 Dec;167(5):608-17

# Objective responses to Brentuximab vedotin as a single agent in DLBCL patients.

| | DLBCL | | | | | | | | | Other B-cell | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Refractory (n = 39) | | | Relapsed (n = 8) | | | Total (n = 48)* | | | Total (n = 19)† | | |
| | No. | % | 95% CI‡ | No. | % | 95% CI‡ | No. | % | 95% CI‡ | No. | % | 95% CI‡ |
| Objective response rate | 17 | 44 | 27.8 to 60.4 | 3 | 38 | 8.5 to 75.5 | 21 | 44 | 29.5 to 58.8 | 5 | 26 | 9.1 to 51.2 |
| Best clinical response§ | | | | | | | | | | | | |
| CR | 6 | 15 | | 2 | 25 | | 8 | 17 | | 3 | 16 | |
| PR | 11 | 28 | | 1 | 13 | | 13 | 27* | | 2 | 11 | |
| SD | 8 | 21 | | 3 | 38 | | 11 | 23 | | 7 | 37 | |
| PD | 14 | 36 | | 2 | 25 | | 16 | 33 | | 6 | 32 | |
| Disease control rate‖ | 25 | 64 | | 6 | 75 | | 32 | 67 | | 12 | 63 | |

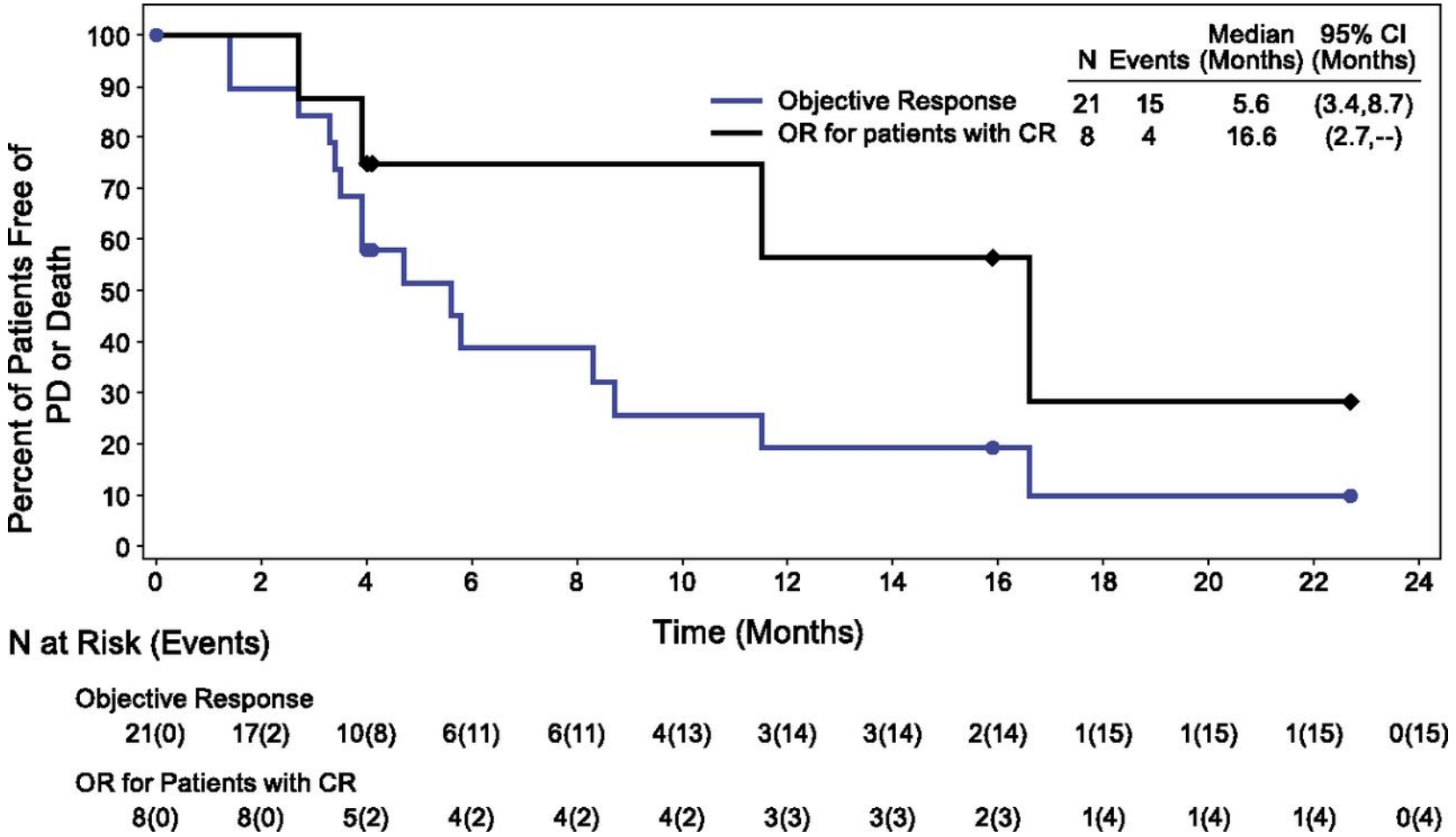
Eric D. Jacobsen et al. Blood 2015;125:1394-1402

# Brentuximab vedotin in DLBCL - Maximum tumor size reduction from baseline.



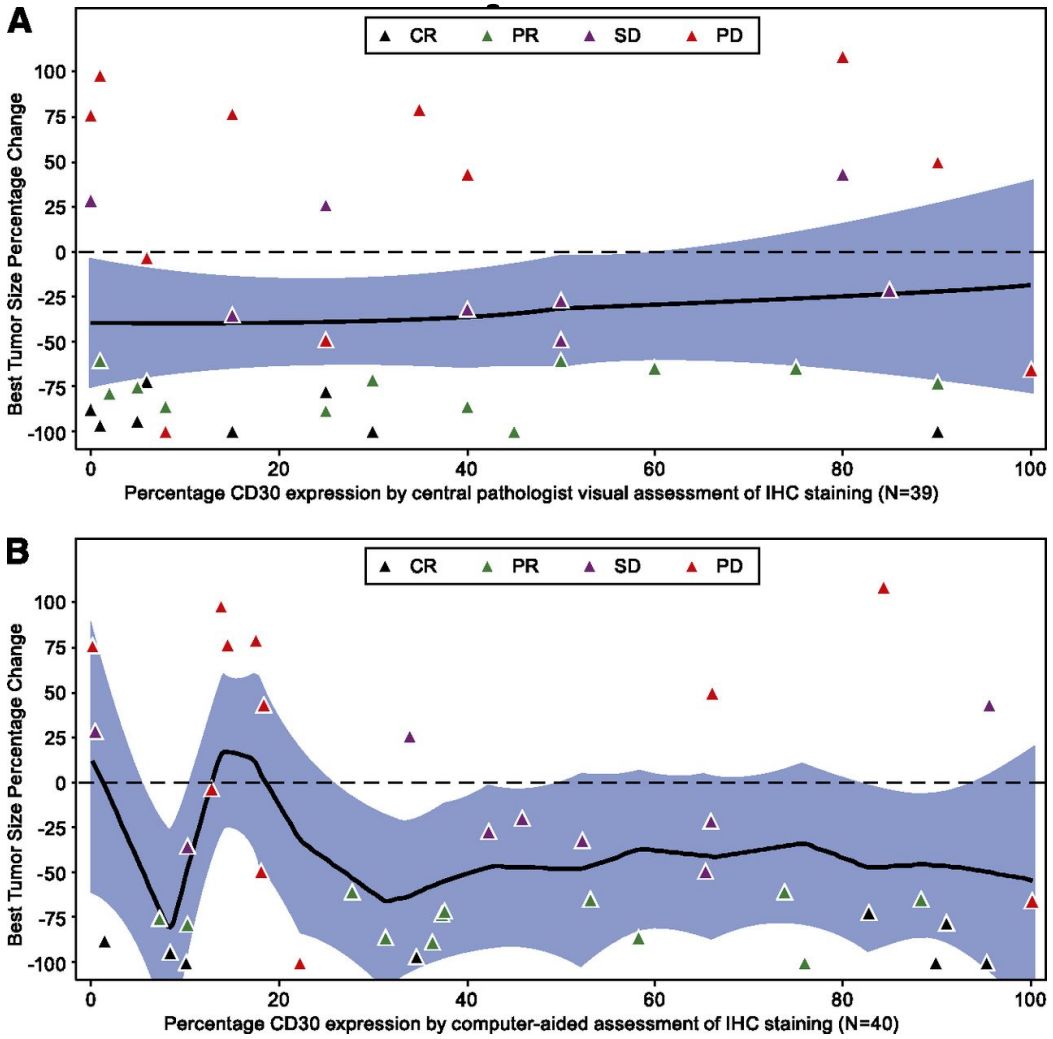

Eric D. Jacobsen et al. Blood 2015;125:1394-1402

# Duration of objective response (OR) and CR in DLBCL patients.



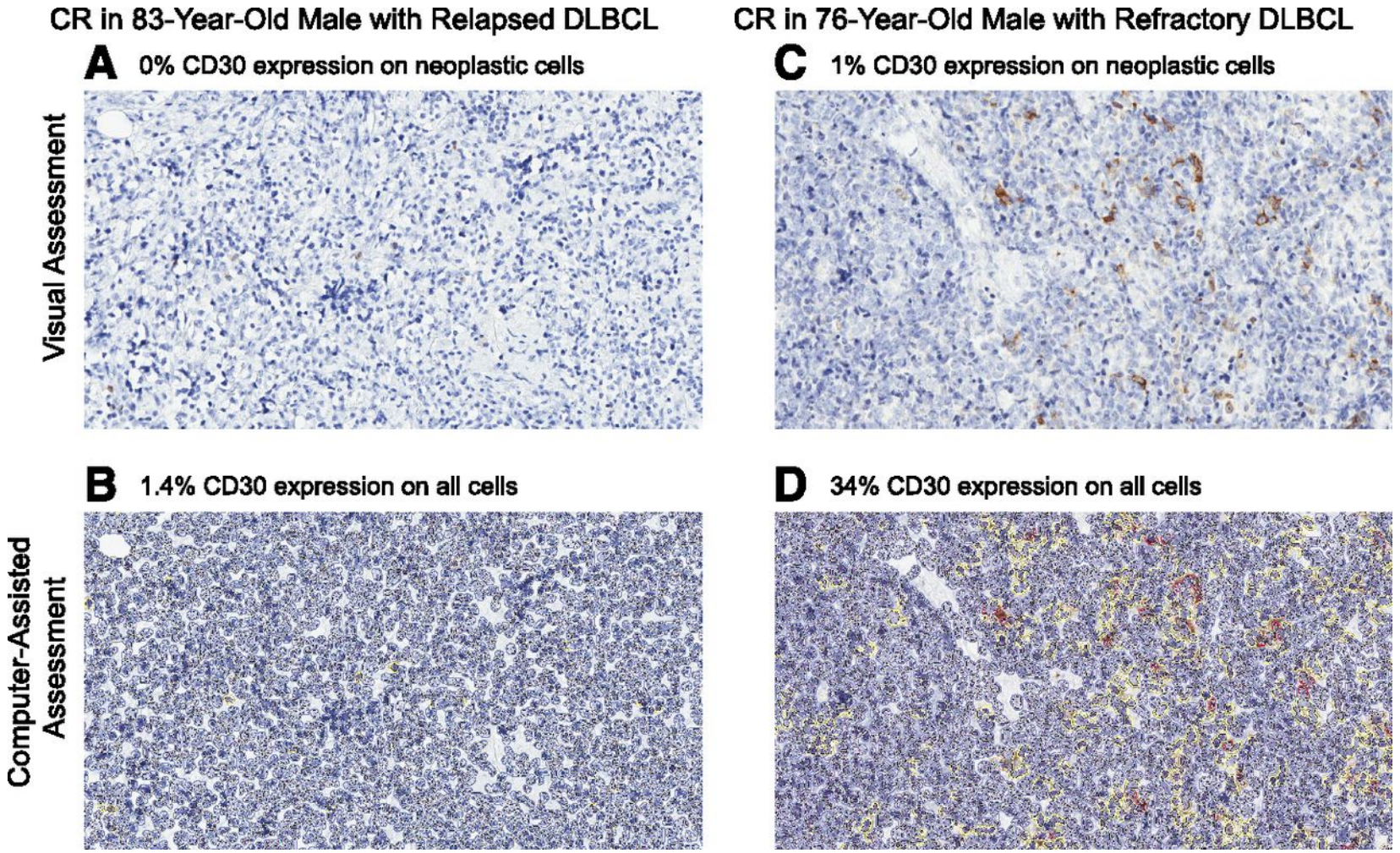

Eric D. Jacobsen et al. Blood 2015;125:1394-1402

# Maximum tumor size reduction by quantitative CD30 expression in DLBCL



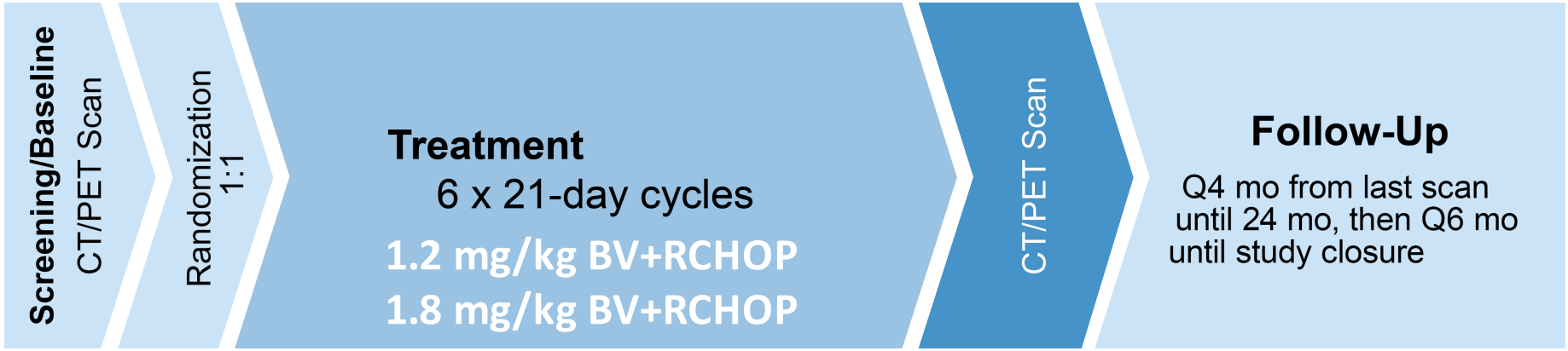

Eric D. Jacobsen et al. Blood 2015;125:1394-1402

# CD30 expression per IHC assessed by visual and computer-assisted methods




Eric D. Jacobsen et al. Blood 2015;125:1394-1402

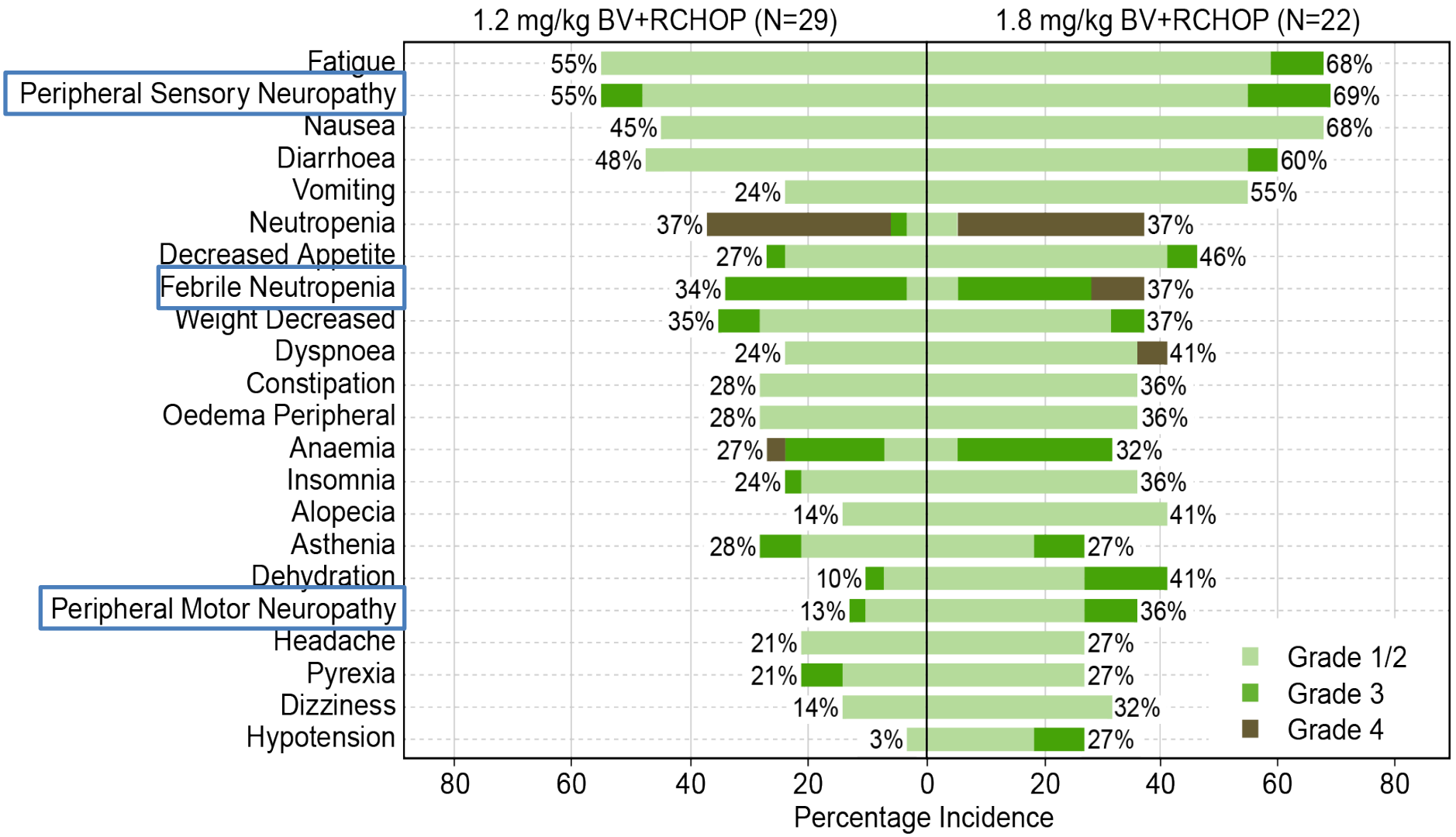
# Brentuximab vedotin plus R-CHOP in DLBCL




Key eligibility criteria included:

- **CD30-unselected high-intermediate or high-risk untreated DLBCL**
- **High-intermediate or high risk**
  - **Standard IPI score 3–5 (>60 years) or**
  - **Age-adjusted IPI [aaIPI] score 2–3 (≤60 years)**
- **ECOG performance status ≤2**

# Treatment-Emergent Adverse Events Grades1–4

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# Antitumor Activity: Dose Cohort

| | 1.2 mg/kg BV+RCHOP N=29 | 1.8 mg/kg BV+RCHOP N=22 | Total N=51 |
|---|---|---|---|
| ORR, % (n) [95% CI] | 79% (23) [60.3, 92.0] | 82% (18) [59.7, 94.8] | 80% (41) [66.9, 90.2] |
| CR, % (n) [95% CI] | 66% (19) [45.7, 82.1] | 68% (15) [45.1, 86.1] | 69% (34) [52.1, 79.2] |
| PR, % (n) | 14% (4) | 14% (3) | 14% (7) |
| PD, % (n) | 7% (2) | 14% (3) | 10% (5) |

**The CR rate was comparable between the ABC subtype and the GCB subtype (69% versus 65%)**

Yasenchak et al ASH 2015 #814

# Progression-Free Survival: Dose Cohort

| | 1.2 mg/kg BV+RCHOP N=29 | 1.8 mg/kg BV+RCHOP N=22 | Total N=51 |
|---|---|---|---|
| PD or death, % (n) | 24% (7) | 41% (9) | 31% (16) |
| Estimated progression-free rate at : | | | |
| 6 months (95% CI) 27 patients at risk | 83% (60, 93) | 75% (49, 89) | 79% (64, 89) |
| 12 months (95% CI) 12 patients at risk | 67% (38, 85) | 61% (34, 80) | 65% (45, 79) |
| Median follow-up time (mo) | 5.4 | 6.0 | 5.7 |

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# Antitumor Activity: CD30 Status

| | CD30-positive N=25 | CD30-negative N=23 |
|---|---|---|
| ORR, % (n) [95% CI] | 84% (21) [44.4, 98.3] | 83% (19) [61.2, 95.0] |
| CR, % (n) [95% CI] | 76% (19) [54.9, 90.6] | 63% (14) [38.5, 80.3] |
| PR, % (n) | 8% (2) | 21% (5) |
| PD, % (n) | 8% (2) | 4% (1) |

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# Progression-Free Survival: CD30 Status

| | CD30-positive N=25 | CD30-negative N=23 |
|---|---|---|
| Patients with PD or death, n (%) | 4 (16) | 9 (39) |
| Estimated progression-free rate at: | | |
| 6 months (95% CI)<br>26 patients at risk | 86% (62, 95) | 81% (56, 92) |
| 12 months (95% CI)<br>12 patients at risk | 82% (62, 95) | 56% (30, 78) |
| Median follow-up time (months) | 8.7 | 6.8 |

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# Conclusions

- Brentuximab vedotin has activity in DLBCL
- Various agents and combinations can be combined with brentuximab vedotin.
- Toxicities will need to be monitored.
- Other ADCs targeting CD19 may take the place of BV in DLBCL.
- Future studies will need a rational approach to decide which combinations are best.