LymphomaHub

DLBCL

# Bendamustine plus ofatumumab for naïve, elderly patients with DLBCL: Results from a phase II trial

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On 9 May 2019, Ian Flinn from the Sarah Cannon Research Institute, Nashville, TN, USA, and colleagues, published diffuse large B-cell lymphoma (DLBCL) phase II clinical trial results (NCT01626352) in *The Oncologist*.[1] This trial investigated the efficacy of bendamustine and ofatumumab in elderly patients with newly-diagnosed DLBCL, who were not good candidates for standard chemotherapy regimens.

The current standard of care for DLBCL is R-CHOP (rituximab, cyclophosphamide, doxorubicin, vincristine, and prednisone) chemotherapy. Nevertheless, old age has been associated with worse outcomes following R-CHOP in patients with DLBCL[2]. Bendamustine in combination with rituximab has shown a more tolerable safety profile in elderly patients than R-CHOP[3]. The anti-CD20 antibody ofatumumab, is also well-tolerated in this population and mediates B-cell lysis.[4] Therefore, this trial sought to examine whether bendamustine plus ofatumumab could be an effective and well tolerated regimen for naïve and elderly DLBCL patients.

The primary endpoint of this single-arm trial was complete response (CR) rate. Secondary endpoints included, overall response rate (ORR), progression-free survival (PFS), overall survival (OS), and safety.

**Study design & baseline characteristics**

- N = 21 enrolled patients with DLBCL, aged ≥ 70 years
- Median patient age (range): 83 (73–88) years
- Male patients: 42.9% (n = 9)
- Dosing (21-day treatment cycles):
  - Bendamustine: 90 mg/m$^2$ intravenously (IV) on Days 1 and 2 of cycles 1–6
  - Ofatumumab: 1000 mg IV on Days 1 and 8 of cycle 1 and on Day 1 of cycles 2–6
- Modified Ann Arbor disease stage at diagnosis:
  - Stage III: 66.7% (n = 14)
  - Stage IV: 33.3% (n = 7)
- Patient race:
  - White: 95.2% (n = 20)
  - American indian/Alaskan native: 4.8% (n = 1)
- Median β2-microglobin levels (range): 3 (0–7)

- Abnormal β2-microglobin levels: 85.7% (n = 18)

**Key findings**

- Median follow-up (range): 9.9 (2.3–4) months

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| ORR, n (%) | 19 (90.5%) |
| Complete response (CR) | 7 (33.3%) |
| Partial response (PR) | 12 (57.1%) |
| Stable disease (SD) | 1 (4.8%) |
| Progressive disease (PD) | 1 (4.8%) |
| Not evaluable | 0 |
| Median PFS (90% CI) | 8.6 months (4.6–10.6) |
| Median OS (90% CI) | 12.0 months (5.9–30.8) |
| Median time-to-progression (TTP; 90% CI) | 10.5 months (4.5–not reached) |

- 12-month OS probability: 52.4% (90% CI, 33.4–3)
- 12-month PFS probability: 31.7% (90% CI, 15.9–8)
- 12-month TTP probability: 40.1% (90% CI, 19.1–4)
- Patients who completed treatment: 57.1% (n = 12)
- Reasons for treatment discontinuation:
  - PD: 14.3% (n = 3)
  - Concurrent illness: 9.5% (n = 2)
  - Death: 9.5% (n = 2; one treatment-related bowel sepsis and one from unknown cause)
  - Patient request: 4.8% (n = 1)
  - Non-compliance: 4.8% (n = 1)

- The study was discontinued early on due to low patient accrual

**Safety**

- Hematological Grade ≥ 3 adverse events (AEs) that occurred:
  - Thrombocytopenia: 14% (n= 3)
  - Neutropenia: 10% (n= 2)
  - Leukopenia: 5% (n = 1)
  - Anemia: 5% (n = 1)
  - Lymphopenia: 5% (n = 1)
- Non-hematological Grade ≥ 3 AEs observed:
  - Vomiting: 10% (n = 2)
  - Diarrhea: 5% (n = 1)
  - Necrosis: 5% (n = 1)
  - Hypomagnesemia: 5% (n = 1)
  - Hyperuricemia: 5% (n = 1)
  - Sepsis: 5% (n = 1)
  - Anorexia: 5% (n = 1)
  - Fatigue: 5% (n = 1)
  - Pneumonia: 5% (n = 1)
  - Hypocalcemia: 5% (n = 1)
  - Hypokalemia: 5% (n = 1)
  - Tumor lysis syndrome: 5% (n = 1)
- Patient deaths at follow-up: 66.7% (n = 14)
  - Reasons of death:
    - Due to AE: 4.8% (n = 1; bowel necrosis)
    - Due to disease: 28.6% (n = 6)
    - Due to concurrent illness: 4.8% (n = 1)
    - Due to unknown causes: 28.6% (n = 6)

**Conclusions**

The results of this small phase II trial showed that the combination of ofatumumab and bendamustine was well tolerated and led to modest response rates in elderly, newly-diagnosed patients with DLBCL. The degree of efficacy may appear modest when compared to standard of care, but maybe of benefit to those intolerant to R-CHOP.

**References**


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