INTRODUCTION

Obinutuzumab (Gazyva®/Gazyvaro®), a F. Hoffmann-La Roche Ltd. G, is a type II glycoengineered humanized monoclonal antibody against the B-lymphocyte transmembrane protein CD20.

GADOLIN (NCT01059630) is a Phase III, multicentre, randomised, open-label, parallel-group, double-blind study comparing the efficacy and safety of G plus bendamustine (B) induction followed by G maintenance (B) with B induction followed by single-agent G maintenance in patients with follicular lymphoma (FL). GADOLIN was conducted in 200 centres across 30 countries. The study assessed MRD negativity at mid-induction (MI) (D1, C1 [PB]), end-of-induction (EOI) (D2, C2 [PB]), and end-of-treatment (EOT) (D8, C6 [PB]) and the association between these MRD results and clinical outcomes. Results of MI and EOI MRD status and kinetics in patients during induction and, for the first time, MRD status post-induction with respect to treatment efficacy and prognostic impact, in patients with FL enrolled in GADOLIN on the basis of the updated efficacy results.2

METHODS

Study design

The GADOLIN study design is presented in Figure 1.3

Table 1. Demographics and baseline characteristics.

<table>
<thead>
<tr>
<th>Category</th>
<th>G-B MRD+ (n=166)</th>
<th>G-B MRD- (n=28)</th>
<th>B MRD+ (n=52)</th>
<th>B MRD- (n=28)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>64.5 (2.7)</td>
<td>66.5 (2.1)</td>
<td>66.2 (2.3)</td>
<td>66.8 (2.2)</td>
</tr>
<tr>
<td>Female (%)</td>
<td>54 (31.1%)</td>
<td>43 (15.3%)</td>
<td>26 (49.2%)</td>
<td>14 (50.0%)</td>
</tr>
<tr>
<td>Ann Arbor stage (n=183)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>I</td>
<td>11 (13%)</td>
<td>7 (25%)</td>
<td>5 (9.6%)</td>
<td>7 (25%)</td>
</tr>
<tr>
<td>II</td>
<td>13 (15%)</td>
<td>3 (11%)</td>
<td>11 (21.2%)</td>
<td>1 (3.6%)</td>
</tr>
<tr>
<td>III</td>
<td>30 (35%)</td>
<td>26 (93%)</td>
<td>3 (5.8%)</td>
<td>22 (85.7%)</td>
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<tr>
<td>IV</td>
<td>16 (18%)</td>
<td>0 (0%)</td>
<td>1 (1.9%)</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>FLIPI, 1 adverse factors (n=209)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ECOC PS (n=227)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0–1</td>
<td>89 (98%)</td>
<td>143 (66%)</td>
<td>31 (36%)</td>
<td>143 (66%)</td>
</tr>
<tr>
<td>2</td>
<td>2 (2%)</td>
<td>13 (6%)</td>
<td>7 (13%)</td>
<td>13 (6%)</td>
</tr>
<tr>
<td>3</td>
<td>10 (10%)</td>
<td>45 (21%)</td>
<td>27 (51.9%)</td>
<td>45 (21%)</td>
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<tr>
<td>4</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
<td>5 (9.4%)</td>
<td>0 (0%)</td>
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<tr>
<td>FLIPI, ≥2 adverse factors (n=209)</td>
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<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0–1</td>
<td>89 (98%)</td>
<td>214 (98%)</td>
<td>31 (36%)</td>
<td>214 (98%)</td>
</tr>
<tr>
<td>2</td>
<td>2 (2%)</td>
<td>2 (2%)</td>
<td>7 (13%)</td>
<td>2 (2%)</td>
</tr>
<tr>
<td>3</td>
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<td>28 (53.8%)</td>
<td>44 (20%)</td>
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<tr>
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<td>0 (0%)</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
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<tr>
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<td>3 (1%)</td>
<td>1 (1.9%)</td>
<td>3 (1.1%)</td>
</tr>
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</table>

MRD analysis

- MRD analysis at MI and EOI confirmed the primary endpoint of GADOLIN, demonstrating that adding G to B induction significantly contributes to the speed and depth of disease response, even though the G-B arm received a lower dose of B than the control arm.
- MRD was a more sensitive measure of efficacy than CT-based tumour response assessment, which did not detect a difference between arms at EOI.
- MRD response identified a prognostically favourable group of patients, while patients without an MRD response at EOI had a very poor prognosis, irrespective of treatment arm.
- After G-B induction, MRD-negative patients appeared to benefit from G maintenance, which potentially prolonged survival, preserved MRD negativity and helped control lymphoma regrowth.

REFERENCES


CONFLICT OF INTEREST

All authors disclose no conflicts of interest.

CONCLUSION

MRD negativity in PB occurred early during induction and was more frequent with G-B (Figure 3B) compared with patients who were MRD-negative at EOI, followed by MRD-positive patients (Figure 5A).

MRD negativity was sustained in many patients who received G-B maintenance (for at least 2 years in some); many patients in the B arm (who received no maintenance) converted back to MRD positivity after EOI (Figure 4).

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