Clinical Use:

Pediatrics: The safety and efficacy of GAZYVA in children (<18 years of age) have not been established.

Contraindications:

• Known hypersensitivity (IgE mediated) to obinutuzumab or to any of the excipients or component of the container.

Most Serious Warnings and Precautions:

Infusion Reactions (IR): GAZYVA can cause severe and life-threatening infusion reactions. Monitor patients closely during infusions. Modify infusion of GAZYVA according to the Grade of reaction.

Hepatitis B Virus (HBV) Reactivation: HBV reactivation, in some cases resulting in fulminant hepatitis, hepatic failure and death, can occur in patients receiving CD20-directed cytolytic antibodies, including GAZYVA.

Progressive Multifocal Leukoencephalopathy (PML): PML can occur in patients receiving GAZYVA. Put GAZYVA treatment on hold in case of PML suspicion, until the diagnosis can be clearly established. Discontinue GAZYVA therapy and consider discontinuation or reduction of any concomitant chemotherapy or immunosuppressive therapy in patients who develop PML.

Tumour Lysis Syndrome (TLS): Serious TLS, including acute renal failure, has been reported in patients receiving GAZYVA.

Cardiovascular: Serious cardiac events, including worsening of existing underlying cardiac disease and fatal cases, such as fatal myocardial infarctions, have been reported with GAZYVA therapy.

Other Relevant Warnings and Precautions:

• To improve traceability of biological medicinal products, the trade name of the administered product and batch number should be clearly recorded (or stated) in the patient file.

• Serious cases of gastrointestinal perforation
• Neutropenia (severe and life threatening)
• Thrombocytopenia (severe and life threatening)
• B-cell depletion
• Hypersensitivity reactions including anaphylaxis
• The safety of immunization with live or attenuated viral vaccines, following GAZYVA therapy has not been studied and vaccination with live virus vaccines is not recommended during treatment and until B-cell recovery
• Serious bacterial, fungal and new or reactivated viral infections (fatal)
• Use in pregnant and/or nursing women; use effective contraception during and for 18 months following treatment
• Exposure in utero to GAZYVA and vaccination of infants with live virus vaccines
• The safety and efficacy of Gazyva in children below 18 years of age have not been established
• Caution should be used when treating the elderly (≥65 years of age) with GAZYVA
• Use in patients with renal impairments
• GAZYVA has not been studied in patients with hepatic impairment
• Patients experiencing infusion-related symptoms should not drive or use machines until symptoms abate

For More Information:

Please consult the Product Monograph at www.roche.com/PMs/Gazyva/Gazyva_PM_E.pdf for important information relating to adverse reactions, interactions and dosing information which have not been discussed in this piece. The Product Monograph is also available by calling Roche Drug Information at 1-888-762-4388.

REFERENCES:


If you require this information in an accessible format, please contact Roche at 1-800-561-1759.

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GAZYVA® (obinutuzumab)

GAZYVA in combination with bendamustine followed by GAZYVA monotherapy is indicated for the treatment of patients with follicular lymphoma who relapsed after, or are refractory to, a rituximab-containing regimen.
GAZYVA in combination with bendamustine, followed by GAZYVA monotherapy, is an option for patients with follicular lymphoma who have relapsed after, or are refractory to, a rituximab-containing regimen.

GAZYVA + BENDAMUSTINE, FOLLOWED BY GAZYVA MONOTHERAPY DEMONSTRATED:

52% reduction in the risk of disease progression, relapse or death from any cause (n=155) vs bendamustine monotherapy (n=166) based on IRC-assessed median PFS (NR vs 13.8 months; HR: 0.48 [95% CI: 0.34–0.68] p<0.0001 at median observation time of 22 months)

SECONDARY ENDPOINT

2x More than doubled median investigator-assessed PFS (n=155) vs bendamustine monotherapy (n=166) (29.2 months vs 13.7 months; HR: 0.48 [95% CI: 0.35–0.67])

SECONDARY ENDPOINT

64% longer median duration of response (n=155) vs bendamustine monotherapy (n=166) (NR vs 11.9 months; HR: 0.36 [95% CI: 0.24–0.54] at median observation time of 22 months)

DEMONSTRATED SAFETY PROFILE:

<table>
<thead>
<tr>
<th>Adverse event</th>
<th>GAZYVA + bendamustine† n=194</th>
<th>Bendamustine n=198</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>All grades (%)</td>
<td>Grades 3–5 (%)</td>
</tr>
<tr>
<td>Infusion-related reactions</td>
<td>69%</td>
<td>11%</td>
</tr>
<tr>
<td>Neutropenia</td>
<td>35%</td>
<td>33%</td>
</tr>
<tr>
<td>Fatigue</td>
<td>29%</td>
<td>2%</td>
</tr>
<tr>
<td>Cough</td>
<td>26%</td>
<td>-</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>23%</td>
<td>1%</td>
</tr>
<tr>
<td>Constipation</td>
<td>19%</td>
<td>-</td>
</tr>
<tr>
<td>Pyrexia</td>
<td>18%</td>
<td>1%</td>
</tr>
<tr>
<td>Thrombocytopenia</td>
<td>14%</td>
<td>10%</td>
</tr>
<tr>
<td>Decreased appetite</td>
<td>14%</td>
<td>2%</td>
</tr>
<tr>
<td>Vomiting</td>
<td>13%</td>
<td>2%</td>
</tr>
<tr>
<td>Upper respiratory tract infection</td>
<td>13%</td>
<td>2%</td>
</tr>
<tr>
<td>Sinusitis</td>
<td>12%</td>
<td>1%</td>
</tr>
<tr>
<td>Arthralgia</td>
<td>12%</td>
<td>-</td>
</tr>
<tr>
<td>Anemia</td>
<td>11%</td>
<td>7%</td>
</tr>
<tr>
<td>Asthenia</td>
<td>11%</td>
<td>1%</td>
</tr>
<tr>
<td>Urinary tract infection</td>
<td>10%</td>
<td>3%</td>
</tr>
</tbody>
</table>

Adapted from GAZYVA Product Monograph.

IRC: Independent review committee.
NR: Not reached.
PFS: Progression-free survival.
* Results from a phase II, open-label, multicentre, randomized and controlled trial in which 396 patients with indolent non-Hodgkin lymphoma (81% with follicular lymphoma) who had no response to or who progressed during or up to 6 months after treatment with rituximab or a rituximab-containing regimen. Patients were randomized 1:1 to receive either bendamustine alone (n=202) or GAZYVA in combination with bendamustine (n=194) for 6 cycles, each of 28 days duration. Patients in the GAZYVA plus bendamustine arm who did not have disease progression at the end of 6th cycle continued receiving GAZYVA monotherapy until disease progression or for up to two years, whichever occurred first.
† Followed by GAZYVA monotherapy.