POLARIX: a phase 3 study of polatuzumab vedotin plus R-CHP versus R-CHOP in patients with untreated DLBCL

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R-CHOP is the frontline treatment for DLBCL

An unmet need remains for patients with previously untreated DLBCL

COO, cell of origin; R-CHOP, rituximab, cyclophosphamide, doxorubicin, vincristine, and prednisone

Failure to improve on R-CHOP

**Intensified chemotherapy**
R-CHOP14, DA-EPOCH-R, R-ACVBP

**Optimised anti-CD20**
More rituximab, obinutuzumab

**Maintenance therapy**
Rituximab, everolimus, lenalidomide, enzastaurin

**Novel agents in combination with R-CHOP**
Bortezomib, ibrutinib, lenalidomide

R-CHOP, rituximab, cyclophosphamide, doxorubicin, vincristine, and prednisone;
DA-EPOCH-R, dose-adjusted etoposide, prednisone, vincristine, cyclophosphamide, doxorubicin, and rituximab; R-ACVBP, rituximab, doxorubicin, cyclophosphamide, vindesine, bleomycin and prednisone

Goy A. J Clin Oncol 2017;35:3519–22
Polatuzumab vedotin: An ADC for DLBCL

Polatuzumab vedotin has demonstrated efficacy in R/R DLBCL in combination with rituximab\(^1,2\) and rituximab-bendamustine\(^3\)

**Treatment** | **Best overall response**
---|---
Pola +/- rituximab | 51–56%\(^1,2\)
Pola + rituximab + bendamustine | 68%\(^3\)

ADC, antibody-drug conjugate; MMAE, monomethyl auristatin E

In frontline: Pola-R-CHP in a phase 1b/2 trial

1. The safety and tolerability of pola-R-CHP is similar to that of R-CHOP

2. Tumour responses to pola-R-CHP assessed by PET

   - Complete response: 77%
   - Partial response: 12%
   - Non-responders: 11%

3. PFS in patients with 1L DLBCL receiving pola + R/G-CHP

   - PFS at 2 years: 83% (95%CI: 73–93%)

G, obinutuzumab; R-CHP, rituximab, cyclophosphamide, doxorubicin, and prednisone; R-CHOP, rituximab, cyclophosphamide, doxorubicin, vincristine, and prednisone

In frontline: Pola-R-CHP in a phase 1b/2 trial

PFS by cell of origin

- ABC (n=16)
- GCB (n=28)
- Unclassified (n=7)

PFS by double expression of MYC and BCL2

- BCL2/MYC negative (n=28)
- BCL2/MYC positive (n=13)

ABC, activated B cell; GCB; germinal centre B cell

In frontline: Pola-R-CHP in a phase 1b/2 trial

PFS by CD79b expression

**POLARIX: Study design**

A double-blind, phase 3, placebo-control trial

### Patients
- Previously untreated DLBCL
- Age 18–80 years
- IPI 2–5
- ECOG PS 0–2

### Stratification factors
- IPI score (2 vs 3–5)
- Bulky disease (≥7.5cm)
- Geographical region

<table>
<thead>
<tr>
<th>ARM A</th>
<th>Polatuzumab vedotin 1.8mg/kg</th>
<th>R-CHP + vincristine placebo Q21D x 6 cycles</th>
</tr>
</thead>
<tbody>
<tr>
<td>ARM B</td>
<td>R-CHOP + pola placebo Q21D x 6 cycles</td>
<td></td>
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</table>

R 1:1

Rituximab 375 mg/m² Cycles 7 and 8

**LYSA, The Lymphoma Study Association;**
**LYSARC, the Lymphoma Academic Research Association**

Collaboration with LYSA and LYSARC
**OBJECTIVE:** To evaluate the efficacy and safety of pola + R-CHP compared with R-CHOP in previously untreated patients with DLBCL

<table>
<thead>
<tr>
<th>Primary endpoint</th>
<th>• PFS*</th>
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</table>
| Secondary endpoints‡ | • PET/CT-CR rate at end of treatment (IRC)  
|                   | • Event-free survival  
|                   | • Overall survival  
|                   | • Patient reported outcomes |
| Safety endpoints‡ | • Incidence, nature, and severity of adverse events |

*Investigator assessed; ‡These lists are not exhaustive
## POLARIX: Treatment and assessment schedule

<table>
<thead>
<tr>
<th>Drug order</th>
<th>Dose</th>
<th>Cycles 1–6</th>
<th>Cycles 7 and 8</th>
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</thead>
<tbody>
<tr>
<td>Prednisone</td>
<td>100 mg/day</td>
<td>■</td>
<td>■</td>
</tr>
<tr>
<td>Rituximab</td>
<td>375 mg/m²</td>
<td>■</td>
<td></td>
</tr>
<tr>
<td>Blinded polatuzumab vedotin or placebo</td>
<td>1.8 mg/kg</td>
<td>■</td>
<td></td>
</tr>
<tr>
<td>Blinded vincristine or placebo</td>
<td>1.4 mg/m² (max 2 mg)</td>
<td>■</td>
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</tr>
<tr>
<td>Cyclophosphamide and doxorubicin</td>
<td>750 mg/m² and 50 mg/m²</td>
<td>■</td>
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<tr>
<td>PET-CT/CT at screening, after 4 cycles and 6–8 weeks after treatment ends</td>
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<tr>
<td>CT scans are performed every 6 months during the first two follow-up years; and then every 12 months in years 3–5 of follow-up</td>
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</tbody>
</table>
POLARIX: Enrolling countries

Europe
- Austria
- Belgium
- Czech Republic
- France
- Germany
- Italy
- Poland
- Portugal
- Russia
- Spain
- Switzerland
- Turkey
- United Kingdom
- Ukraine

North America
- Canada
- USA

South America
- Brazil

APAC
- Australia
- Hong Kong
- S. Korea
- New Zealand
- Taiwan
- Japan
- China
Conclusions

• Polatuzumab vedotin is a first-in-class anti-CD79b antibody-drug conjugate; CD79b is ubiquitously expressed on tumour cells in patients with DLBCL

• In a phase II study, polatuzumab vedotin has exhibited clinical activity and manageable safety profile when delivered in combination with R-CHP in frontline DLBCL

• The POLARIX study is actively enrolling with a primary endpoint of investigator-assessed PFS
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