

Assessing a ctDNA and PET-oriented therapy in patients with DLBCL multicenter, open-label, phase II trial

Despite advances in the clinical care of patients with DLBCL and in understanding the biology of this disease, cure rates have remained the same since the introduction of rituximab to CHOP chemotherapy, and RCHOP chemoimmunotherapy remains the standard of care. Over the last years many phase III trials investigating new agents added to R-CHOP have been performed but they have all invariably failed to improve treatment outcomes. Importantly, three of the most recently completed phase III trials that were developed based on the cell of origin distinction of DLBCL and aimed to improve treatment outcome in the ABC (or non- Germinal center B-Cell (GCB)) subtype by adding a targeted agent to R-CHOP have also failed. This provides clinical evidence that cell of origin may not be an accurate biomarker for treatment decisions. The R – CHOP + investigational drug approach has thus failed either when broadly applied to unselected DLBCL patients or when applied to DLBCL patients selected according to inaccurate biomarkers such as COO.

Within this exploratory multicohort phase II trial, we aim to evaluate a PET_CT and ctDNA oriented therapy in DLBCL in order to test the following working hypothesis.

- acalabrutinib-R-CHOP may improve the progression free survival in genetically defined DLBCL harboring the MYD88 L265P and/or CD79A/B mutations;
- treatment escalation to acalabrutinib-R-CHOP in DLBCL patients who have positive PET/CT (with residual disease scored as Deauville score 4) and no molecular response ($2\log_{10}$ reduction of ctDNA) after two R-CHOP, could improve the anti-tumour activity of R-CHOP;
- treatment de-escalation to 4 total R-CHOP courses plus 2 rituximab single agent infusions does not compromise the outcome in patients lacking both MYD88 L265P and CD79A/B mutations and quickly obtaining both negative PET/CT (Deauville score 1-3) and molecular response ($>2\log_{10}$ reduction of ctDNA) after two R-CHOP, and further improve to Deauville score 1-2 and absence of ctDNA after two more R-CHOP courses

project members

keywords

ctDNA and PET-oriented therapy, patients with
DLBCLA

type of project

clinical studies

status

ongoing - recruiting phase

start of project

2021

end of project

2030

study design

Phase II

Swissmedic notification number2020DR2167

responsible person

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