# Sequential Treatment with Rituximab and CHOP Chemotherapy in B-Cell PTLD: Results from a Multicenter Phase II Trial

Trappe R et al.
*Proc ASH* 2009;Abstract 100.

# Introduction

- Post-transplant lymphoproliferative disorder (PTLD) is associated with the use of immunosuppressive drugs following transplantation (*Transplant Proc* 1969;1:106)
- Immunosuppression reduction (IR) is the initial therapy for PTLD (*Transplantation* 2008;86:215).
- A Phase II trial was initiated in January 2003 to assess sequential treatment with rituximab (R) and CHOP-21 in patients with PTLD unresponsive to IR (*Proc ASH* 2007;Abstract 390).
- Current study objective:
  - Report on the interim analysis of safety and efficacy from a study of sequential treatment (ST) with R and CHOP-21 with G-CSF in patients (pts) with PTLD unresponsive to IR.
  - Protocol amended to evaluate therapy based on risk stratification.

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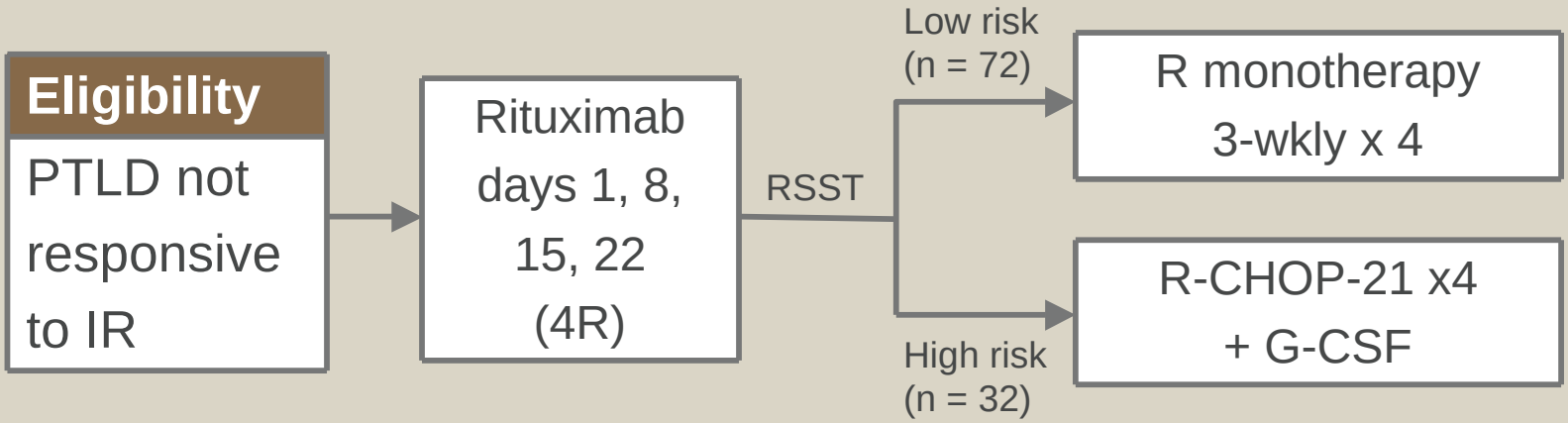
# Modified Phase II Study Design Including Risk Stratification*




- Low Risk = Complete remission
- High Risk = Partial response, stable disease or progressive disease

* Initially, treatment was sequential (ST): 4R ➔ CHOP-21 x 4. The protocol was amended in 2007 to introduce risk stratification (RSST) after interim analysis showed response to R predicted overall survival (OS).

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# Patient Characteristics

| Characteristic | ST | RSST |
|---|---|---|
| Median age, years | 53 | 60 |
| Advanced stage (Ann Arbor III/IV), % | 59 | 58 |
| Monomorphic or (Polymorphic) PTLD, n | 61 (3) | 35 (5) |
| Transplant recipients | | |
| Kidney/Kidney + Pancreas | 27/3 | 23/0 |
| Liver | 15 | 8 |
| Heart | 13 | 6 |
| Lung OR Heart + Lung | 6 | 3 |
| Epstein-Barr virus positive, % | 49 | 47 |
| Late PTLD (>1 year post-transplant), % | 75 | 75 |

ST = sequential treatment; RSST = risk-stratified sequential treatment

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# Interim Analysis: Efficacy

| Response to 4R | ST and RSST (n = 104)* | |
|---|---|---|
| Overall response (ORR)<br>Complete response (CR) | 54%<br>32% | |
| **Efficacy Parameter** | **ST (n = 64)** | **RSST (n = 40)** |
| Final ORR (%), CR (%) | 89, 69 | 90, 73 |
| No disease progression at years 1, 2, 3 (%) | 86, 75, 75 | 90, —, — |
| Disease-free survival at years 1, 2, 3 (%) | 87, 78, 70 | — |

* Median follow-up, ST = 34 months; RSST = 9.1 months

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# Treatment-Related Deaths

| ST (n = 64) | Patients (n) |
|---|---|
| Cytomegalovirus colitis | 1 |
| Pneumocystis pneumonia | 1 |
| Fulminant hepatitis/sepsis | 1/3 |
| Refractory PTLD | 2 |
| Hemorrhage during treatment | 2 |
| **RSST (n = 40)** | **Patients (n)** |
| Sepsis (due to intestinal perforation) | 1 |

No difference in toxicity was observed between CHOP and R-CHOP in ST/RSST.

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# Conclusions

- Sequential treatment with R and CHOP-21 + G-CSF is well tolerated and highly effective and may improve overall survival in patients with PTLD.
  - Treatment-related mortality: <10%; ORR up to 90%
- Compared to historic series of R monotherapy, more patients achieve complete remission and prolonged TTP with ST.
- Compared to historic series of CHOP chemotherapy, ST is better tolerated. This may be due to lower tumor burden and better patient fitness at the time of chemotherapy.
- Use of RSST according to response to 4 courses of R might improve overall response, tolerability and overall survival:
  - Chemotherapy limited to patients at high risk.
  - R monotherapy extended for patients at low risk.

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# Faculty Comments

**DR VOSE:** This is the largest prospective study of a common type of treatment used for PTLD. The population studied had several mixed patient populations including both monomorphic and polymorphic PTLD and patients having different types of solid organ transplants. Median age at diagnosis was 53 years, and most patients had advanced-stage disease. Approximately half the patients were EBV-positive, and about 75 percent of patients had late PTLD. The overall response to four initial courses of rituximab was 54 percent, and the rate went up with CHOP or R-CHOP to 89 percent with a 69 percent CR rate. These rates compare favorably to historical information using other types of agents. Although this is already a sort of standard treatment used by physicians, this study outlines well the approach to PTLD, and the results are compelling.