A Phase II Trial of Extended Induction Epratuzumab (anti-CD22 antibody) + Rituximab in Previously Untreated Follicular Non-Hodgkin's Lymphoma: CALGB 50701

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CALGB Studies in Untreated FL

- Low/Intermediate FLIPI
  - CALGB 50402 - Rituximab + galiximab
  - CALGB 50404 - Rituximab + oblimersen
  - CALGB 50701 - Rituximab + epratuzumab
  - CALGB 50803 - Rituximab + lenalidomide
  - CALGB 50901 - Ofatumumab
  - CALGB XXXX - TBD
- High FLIPI
  - B-O vs BVO

CALGB 50701: Background

- Limited prospective information on PET in follicular lymphoma
- No data on PET with biological therapy
- Goal to determine if PET can be used as a surrogate predictor of response for new drug development

50701 Background

- Treatments have improved survival for patients with follicular lymphoma, however chemotherapy and radiation have severe associated toxicities
- Extended induction rituximab schedule used by SAKK effective, used as basis for Phase II combinations
- CD22 is a 135 kDa sialoglycoprotein expressed only on B-cells, and on >90% of follicular lymphomas

50701 Background

- Epratuzumab, a humanized antibody directed at CD22, has single agent efficacy against follicular lymphoma
- Rituximab + epratuzumab combination more effective than either antibody alone in mouse model
- Rituximab + epratuzumab in weekly x 4 schedule for relapsed/refractory lymphoma demonstrate activity against follicular, with 67% RR and 60% CR/CRu and TTP 18 mos
- Toxicities of combination not different from rituximab alone

CALGB 50701: Primary Objectives

- Determine response rate (OR and CR)
- Determine time to progression (TTP)

50701 Rituximab + Epratuzumab
Secondary Objectives

- Define toxicity profile
- Determine whether combination promising enough to warrant phase III comparison with rituximab alone
- Determine correlation between early (day 22-24) change in FDG uptake to RR and TTP
- Correlate Fc receptor profiling with response rate
- Correlate CD22 expression, lymphoma associated macrophages (LAM) and FOXP3 tissue profiling with RR and TTP

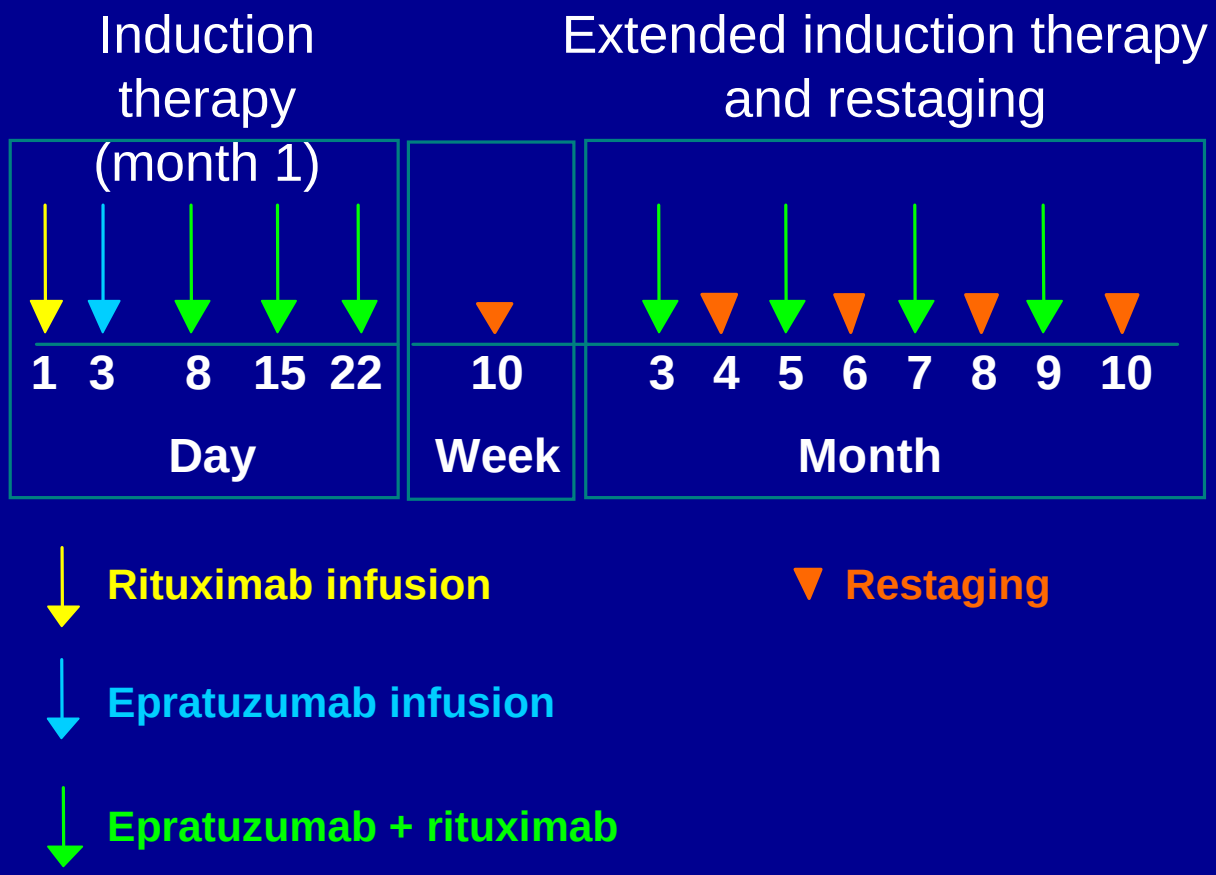
50701 Eligibility Criteria

- Previously untreated, histologically confirmed follicular lymphoma, stage III, IV or bulky stage II (>7cm mass)
- CD20+
- PS 0-2
- Measurable disease

- Low-intermediate risk FLIPI

- Accrual goal 58 patients

CALGB 50701: Treatment Schedule



FDG-PET after 1 cycle

50701 Schema

- **<u>Induction</u>**:
  4 weekly infusions of:
  epratuzumab 360 mg/m^2/dose &
  rituximab 375 mg/m^2/dose

- **<u>Extended Induction:</u>**
  Weeks 12, 20, 28 & 36:
  epratuzumab 360 mg/m^2/dose &
  rituximab 375 mg/m^2/dose

CALGB 50701

- 60 patients registered to the study
- 54 with adequate response data
- 49 with PET data/43 with response data
- Responses
  - Best usually by week 10
  - Some at week 24
  - Early PRs improved to CRs

Correlation Between Δ SUV and Response

- Percent response computed by summing SUVs of all lesions for each patient
- Assessment done pre- and post-tx
- Percent changed using sums of SUVs
- Compared IHP with liver-based PET

Very Preliminary Conclusions

- % change in SUV did not correlate with response (? Liver-based)
- Too early for PFS correlations
- While early PET may predict chemotherapy/immunochemotherapy, it does not appear to predict immunotherapy response

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