# Moxetumomab Pasudotox for Advanced Hairy Cell Leukemia
## (enrollment anticipated in 2018)

**Eligibility:**

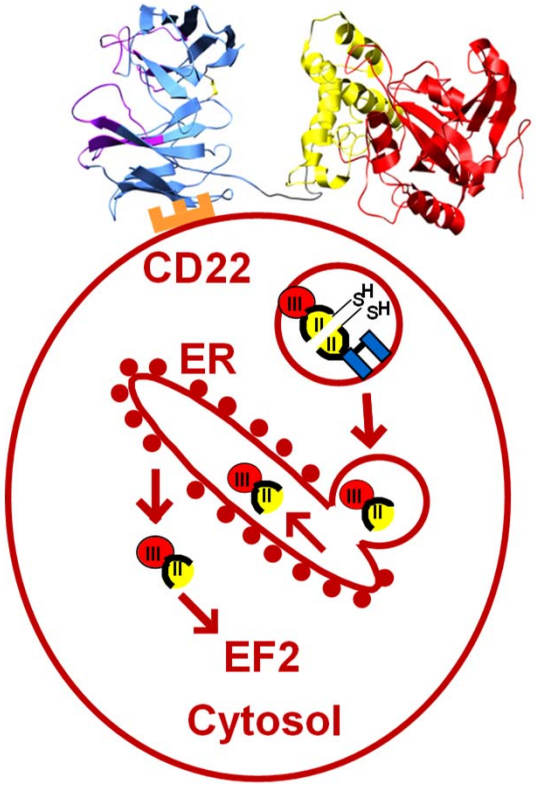
- At least 2 prior treatments, including purine analog.
- Need for treatment (low blood counts or spleen pain)
- No prior recombinant toxin
- Hairy cell leukemia variant (HCLv) accepted

**Rationale**

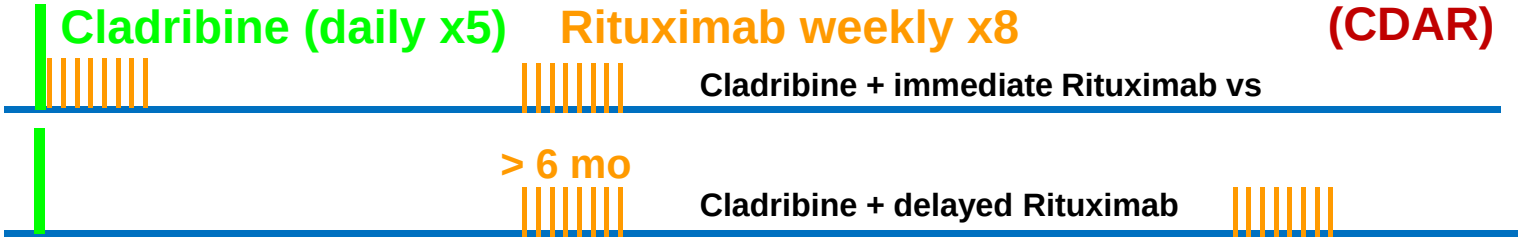
- Moxetumomab pasudotox, formally called HA22 or CAT-8015, is a recombinant immunotoxin made out of 2 parts, an antibody part binding to CD22 on B-cells, and a toxin part (domain II and III) which kills the cell.
- The toxin is extremely potent, only 1 molecule in the cytoplasm is enough to kill a cell.
- HCL cells have much more CD22 than normal B-cells.
- Normal B-cells rapidly regenerate from CD22-negative cells, but HCL cells may not return if eradicated.
- ~50% complete remission (CR) rate at the highest dose level. (https://www.ncbi.nlm.nih.gov/pubmed/22355053).
- Most of these complete remissions (CRs) had no minimal residual disease (MRD) and did not relapse.
- Although severe toxicity was not seen, a low-grade hemolytic uremic syndrome, with temporary decrease in platelets and increase in creatinine, was seen in 2 of 49 patients.

**Design**

- 30 minute iv infusion every other day for 3 doses, repeat every 4 weeks for 6 cycles.
- Patients are then followed without treatment.



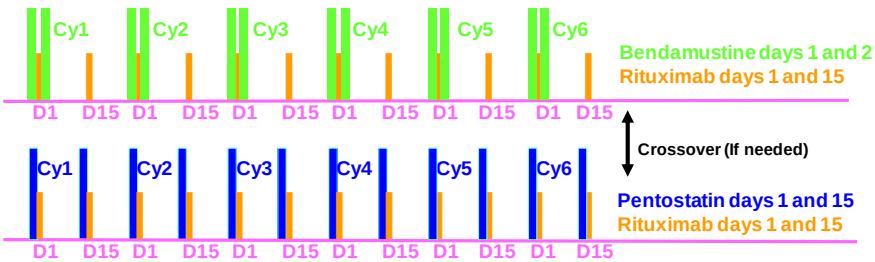

# Cladribine With Simultaneous or Delayed Rituximab for early HCL (CDAR)




- Eligibility: 0-1 prior purine analog, or HCL variant (HCLv), and need for treatment (i.e. low blood counts)
- Minimal residual disease (MRD) after purine analog (cladribine or pentostatin) may cause relapse.
- Immediate or >6-month delayed rituximab guided by MRD measurements each may have advantages over standard therapy, i.e. a 2nd course of purine analog and waiting for relapse.
- All patients get 5 daily doses of cladribine, and get 8 weekly doses of rituximab begun either the 1st day or delayed at least 6 months later when MRD is detectable.
- Patients are followed indefinitely for MRD and the rituximab can be repeated later if needed.

# Rituximab with Either Pentostatin or Bendamustine for Relapsed HCL (BRPR)

- Eligibility: At least 2 prior treatments, including purine analog, need for treatment based on blood counts or spleen pain, HCL or HCLv
- Rationale: Rituximab synergistic with chemo, effective with pentostatin. Bendamustine a purine analog which has additional mechanisms of action and may kill resistant HCL cells.




- Design: Patients receive rituximab (days 1 & 15) and either bendamustine (days 1 & 2) or pentostatin (days 1 & 15). If one option does not work or after relapse, patients may cross over to the other regimen.

# BRAF & MEK Inhibitors Dabrafenib & Trametinib for Hairy Cell Leukemia

**Rationale:**

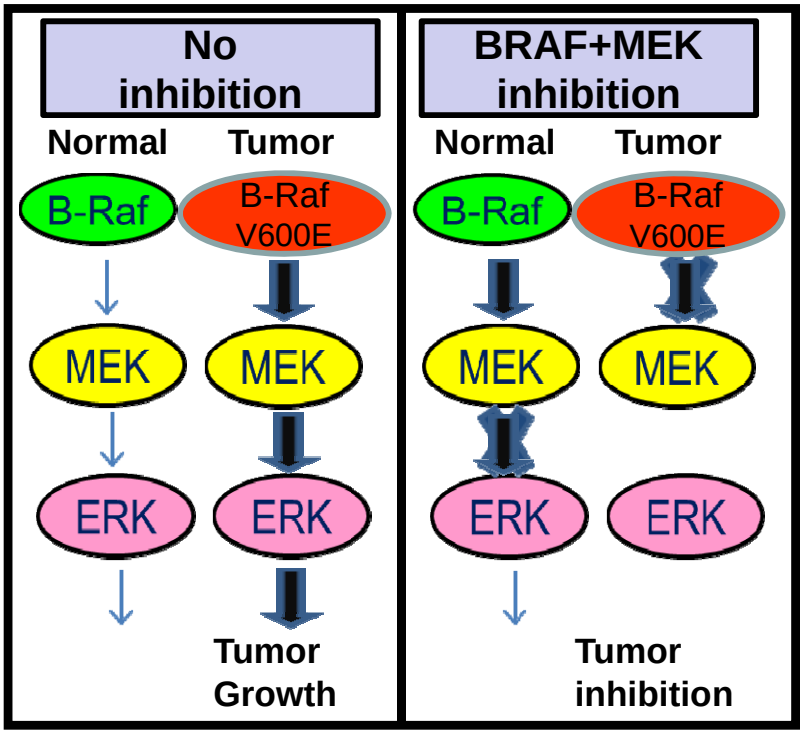
- Classic HCL expresses the BRAF V600E mutation in 85-100% of cases
- The BRAF V600E Inhibitor, Vemurafenib, approved for melanoma, is active in classic HCL, and has been tested at MSKCC and other sites.
- BRAF normally activates MEK, which then activates ERK, which then stimulates cell growth.
- Combined BRAF & MEK inhibition with dabrafenib and trametinib has been effective in and has been approved for certain patients with melanoma.
- The goal of this trial is to determine if BRAF & MEK inhibition will be effective and safe in HCL.

**Eligibility:**

- Classic BRAF V600E+ HCL with at least 2 prior treatments, including purine analog.
- Need for treatment, including low blood counts, large spleen, or infections.

**Design:**

- 2 oral medications, no placebo, monthly visits to look for response and toxicity.




## Multicenter study of BTK inhibitor Ibrutinib for relapsed HCL/HCLv

- Study center is Ohio State University, NIH is one of several participating sites.
- Eligibility: HCL or HCLv, needing treatment: low normal blood counts, large spleen or nodes, infections
- Design: Oral medication, frequent visits to look for response and toxicity.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## HCL/HCLv treatment algorithm (standard & investigational)