Hairy cell leukaemia: Treatment

Why, What and How?

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Why treat Hairy Cell Leukaemia?

Why treat hairy cell leukaemia?

- **Ultimate aim: cure**
  - (but current treatments don't provide that)

- **Survival: to live as long as possible**
  - avoid death from hairy cell leukaemia, complications from the disease or the treatment

- **Good quality life:**
  - for you to carry on doing things that you enjoy doing

Overall survival (how long you live for)

Number of studies looking at outcomes of patients with HCL, show that the average length of time alive is the same as an age-matched population.

Else et al BJH 2009 145(6): 733-740
Bohn et al Cancers 2022 14(5): 1242

What to use to treat hairy cell leukaemia?

When treatments are tested in hairy cell leukaemia?

- Often depth of response is the main endpoint of trials
  (how much of the disease has gone)

  - Blood counts- normal or not
  - Spleen size- normal or not
  - % of hairy cells seen in bone marrow- can they be seen or not

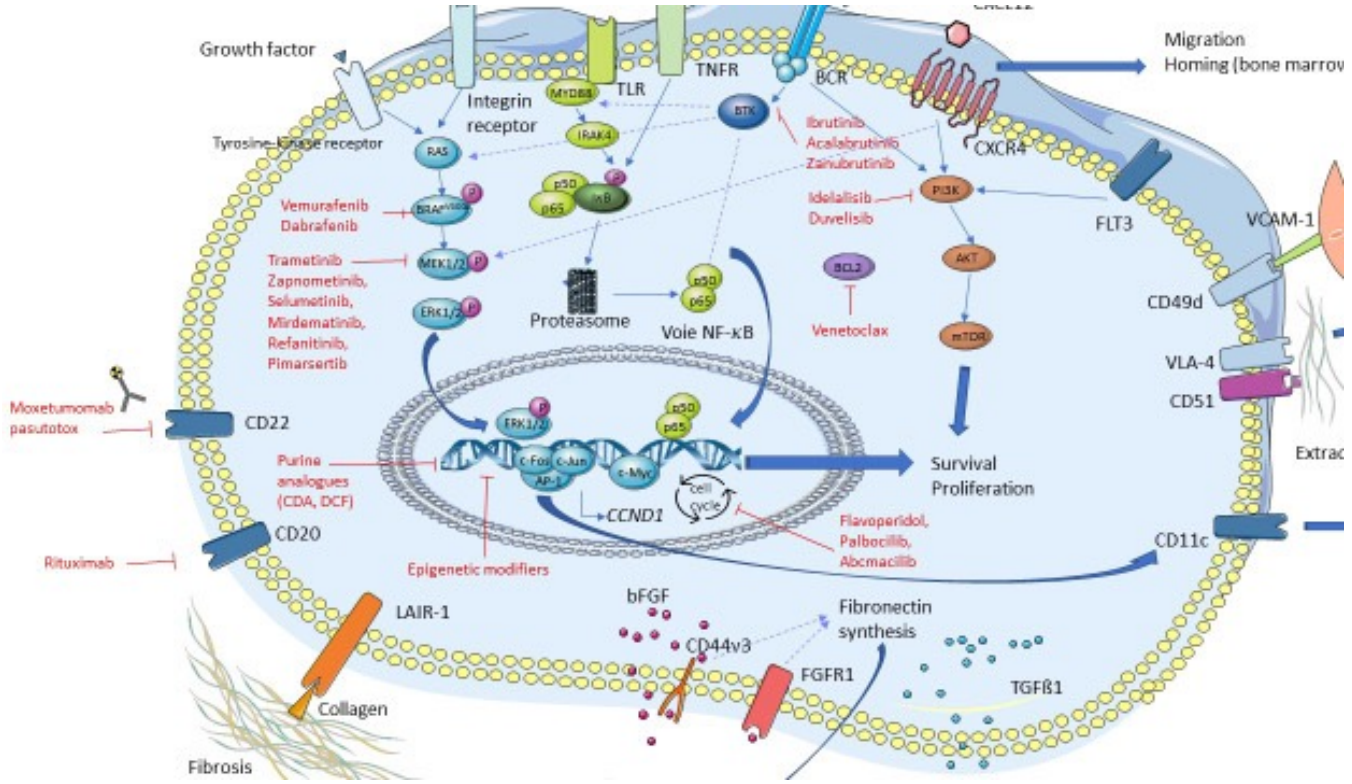
  - MRD (minimal residual disease)- can any hairy cells be detected by very powerful tests that can detect 1 in 10,000 cells.

THESE ENDPOINTS MAY OR MAY NOT CORRELATE WITH ANY OF YOUR GOALS

PROOF OF EFFICACY DOESN'T MEAN THAT THEY AUTOMATICALLY ARE AVAILABLE

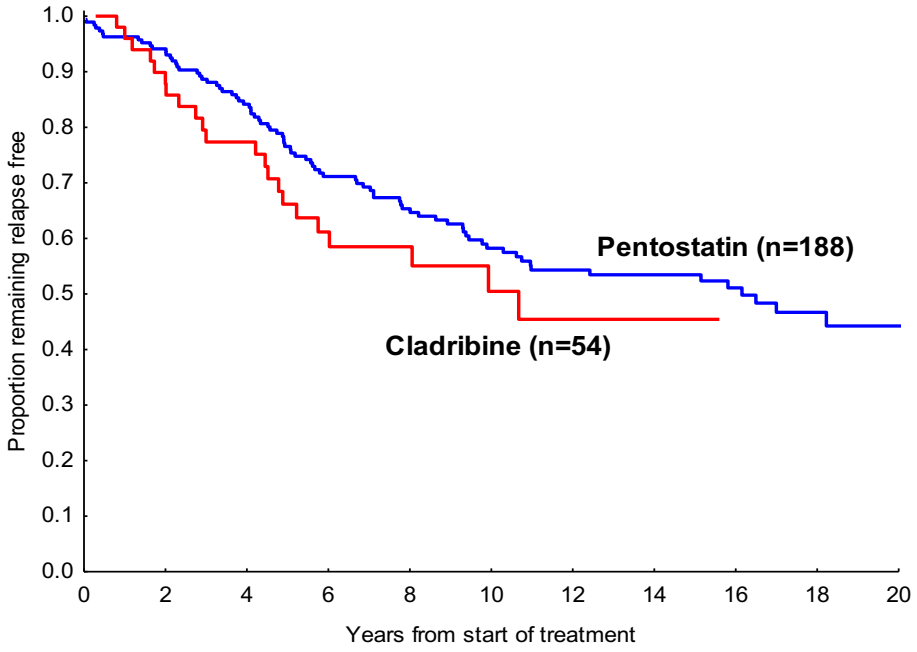
Current treatment options

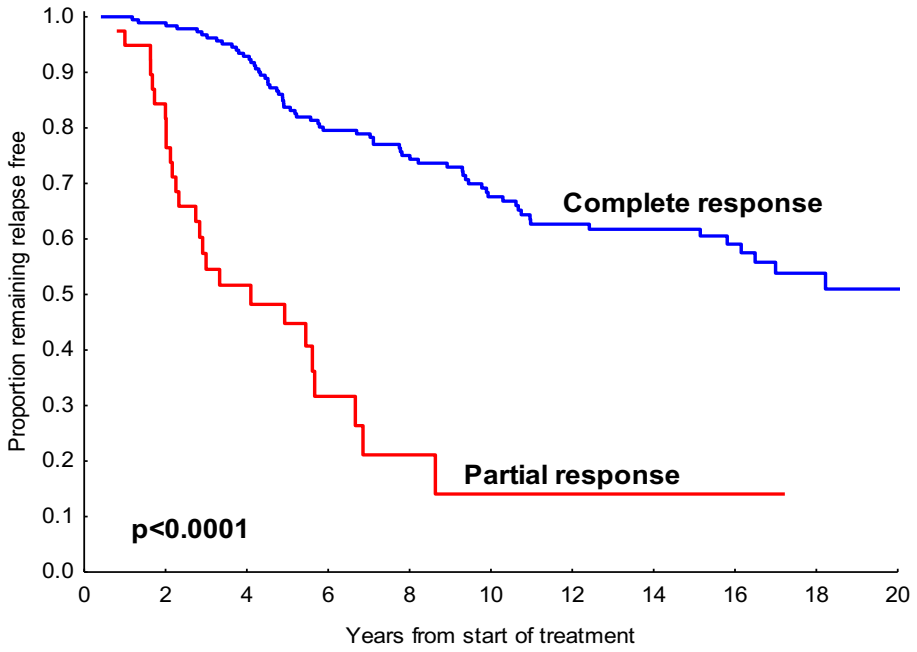
- Active surveillance
- Therapy
  - Chemotherapy (purine analogues)
  - Antibody therapy
  - Targeted therapies
  - Very old therapies- IFN alpha
- Splenectomy (removal of spleen)



Maitre et al Front Oncol. 2022; 12: 1068981

Purine analogues: Cladribine and pentostatin

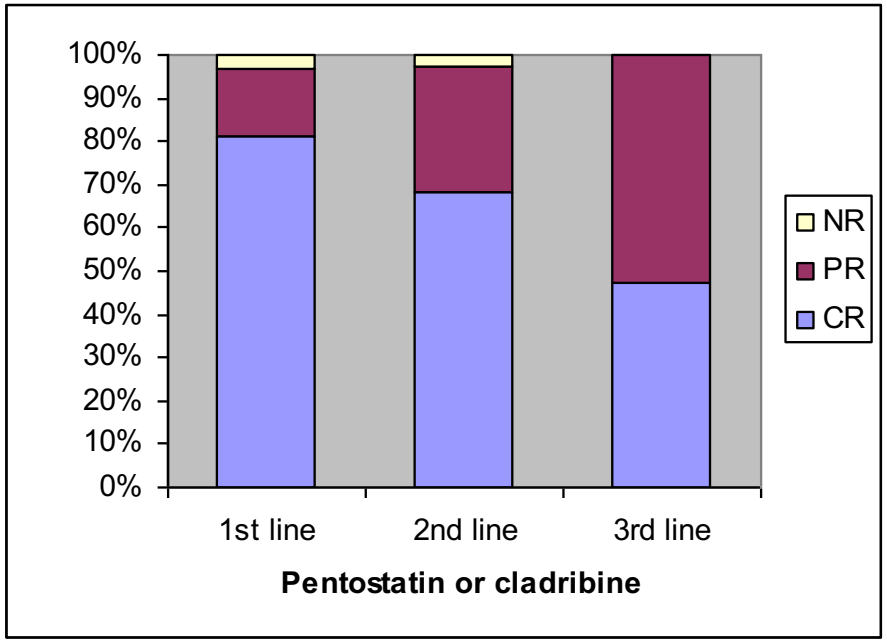




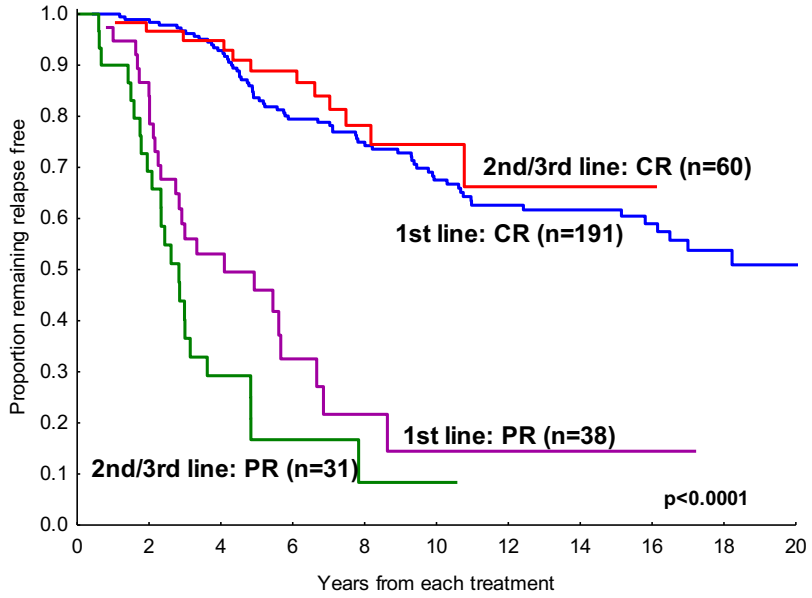
Else *et al*, *Cancer* 104: 2442 (2005) (updated 2010)

Repeated treatment can still be effective, but on average will not last as long.

Response by line of treatment



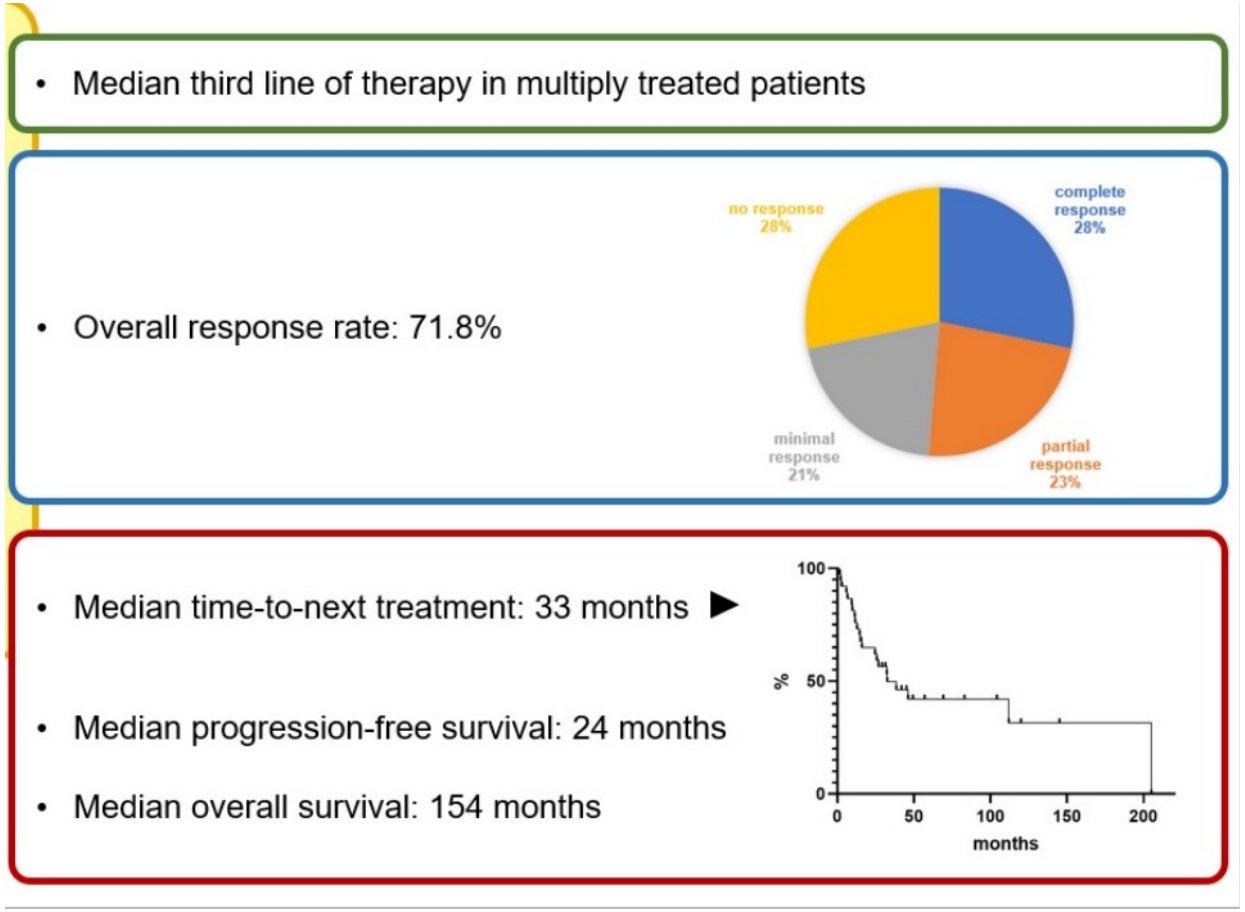
Relapse-Free Survival



- Median time to relapse 16y (1st line), 11y (2nd line), 6.5y (3rd line)

Antibody therapy: Rituximab

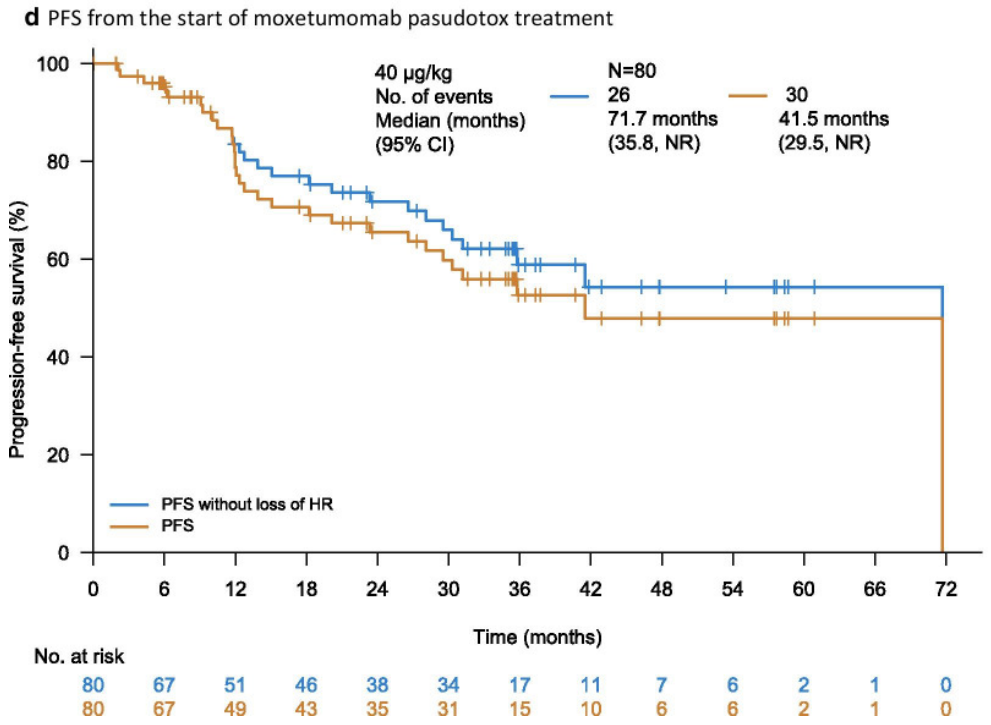
33 patients with hairy cell leukaemia that has come back after treatment (relapsed) or has not responded to treatment (refractory)



Zinzani et al Blood advances 2023

Antibody therapy: Moxetumomab

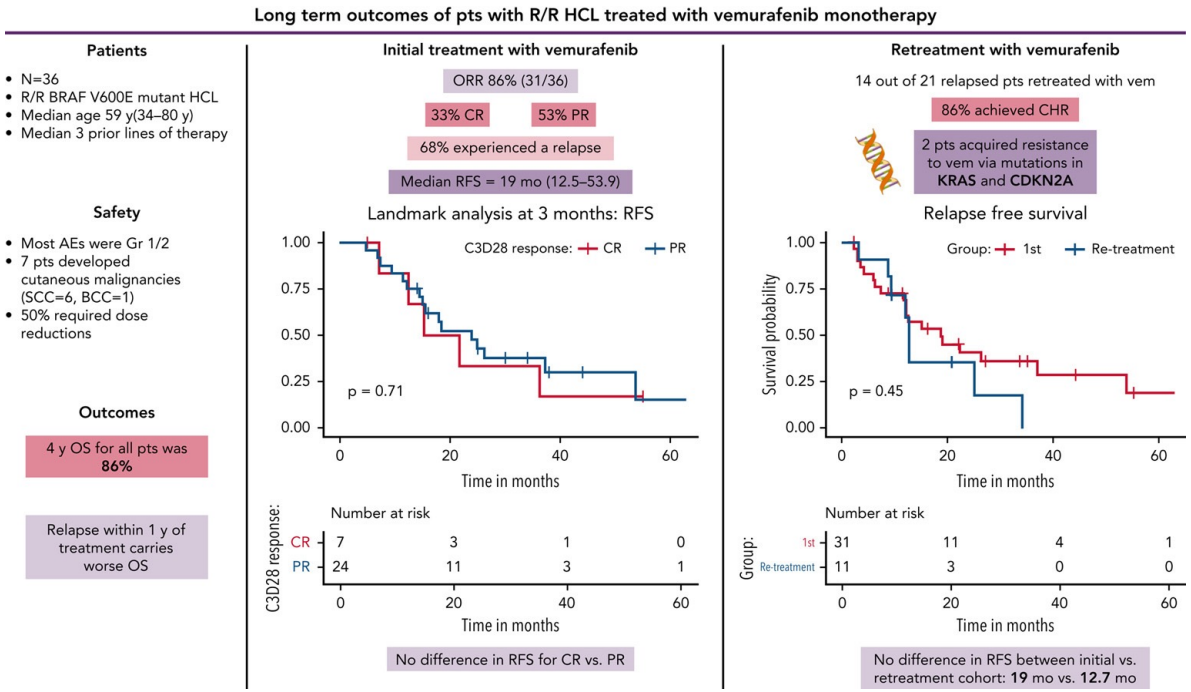
- Antibody targets CD22 with toxin attached to kill the cells
- 36% had durable CR (>180 days)
- Unfortunately no longer available



Kreitman et al J Hematol Oncol. 2021; 14: 35.

Targeted therapies: BRAF inhibitors

- 2 BRAF inhibitors that have been used “extensively” in HCL
  - Dabrafenib and vemurafenib

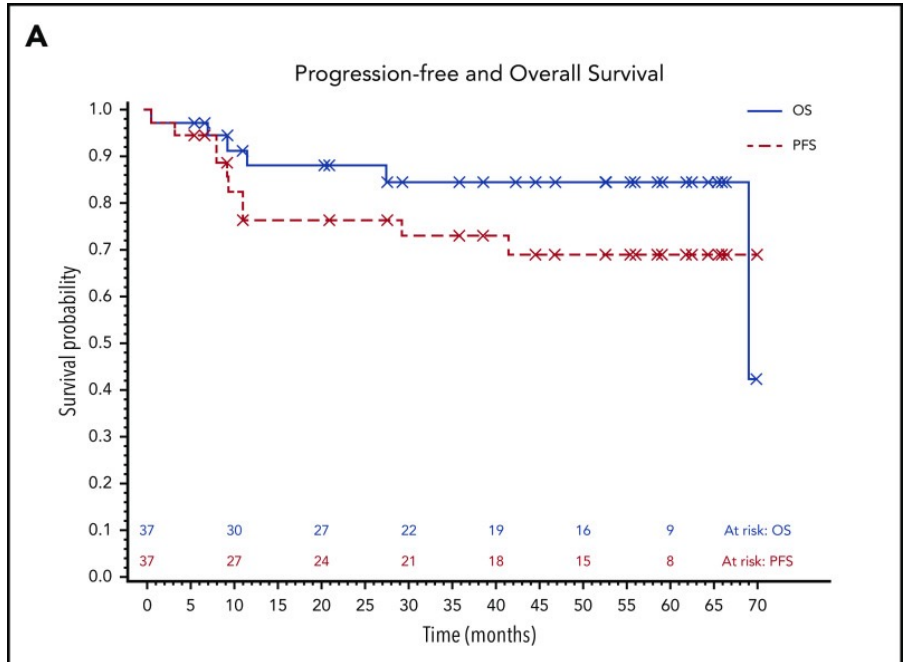


Vemurafenib for 3-6 months

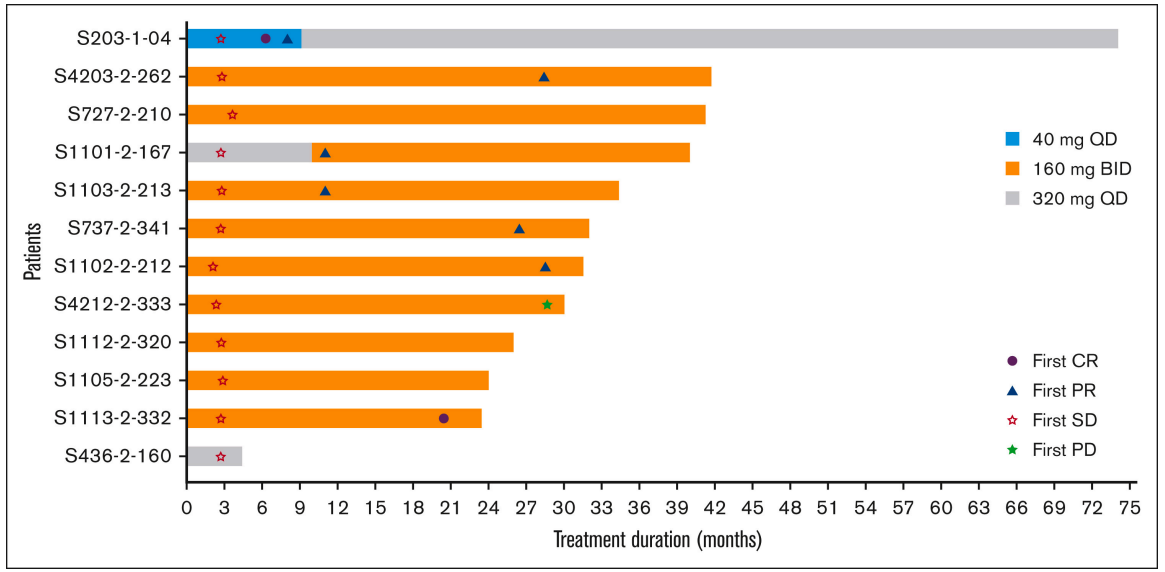
Handa et al Blood 2022 140(25):2663-2671

Targeted therapies: BTK inhibitors

- Used in other B cell cancers
- Ibrutinib and zanubrutinib have been tested in hairy cell leukaemia



Rogers et al. Blood 2021 Jun 24;137(25):3473-3483



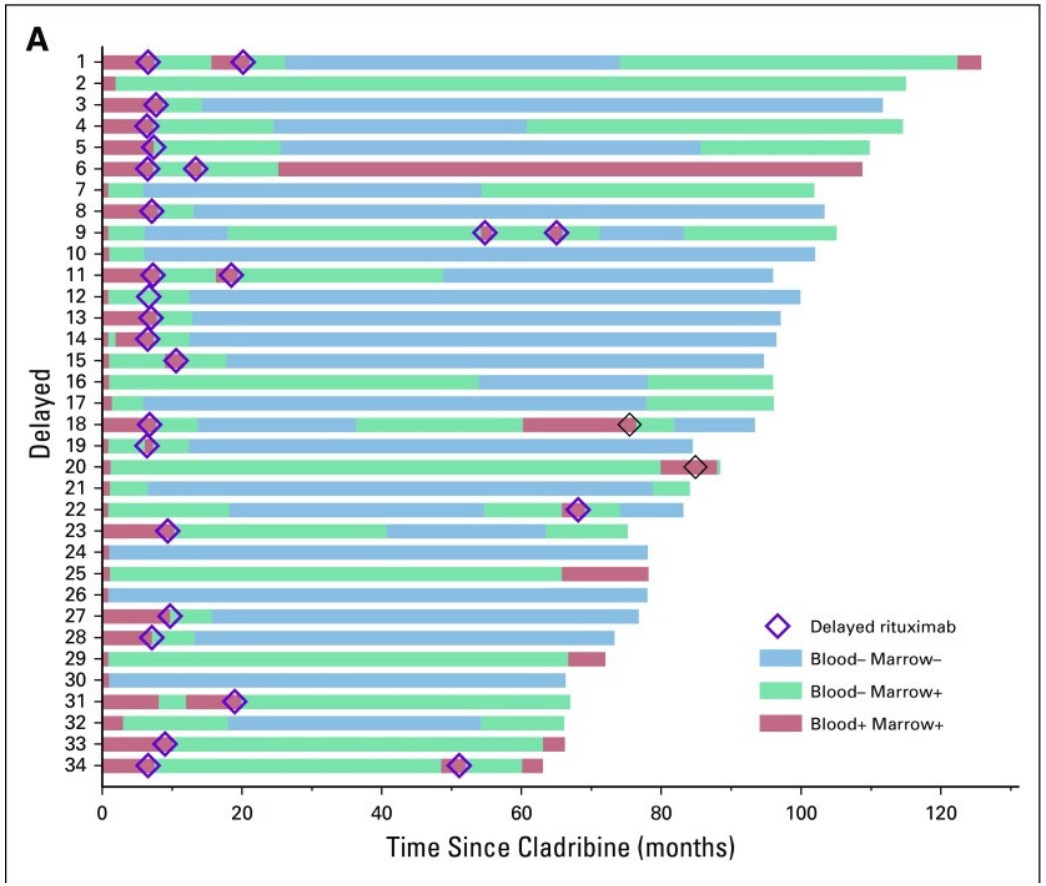
Tam et al Blood Adv (2023) 7 (12): 2884–2887

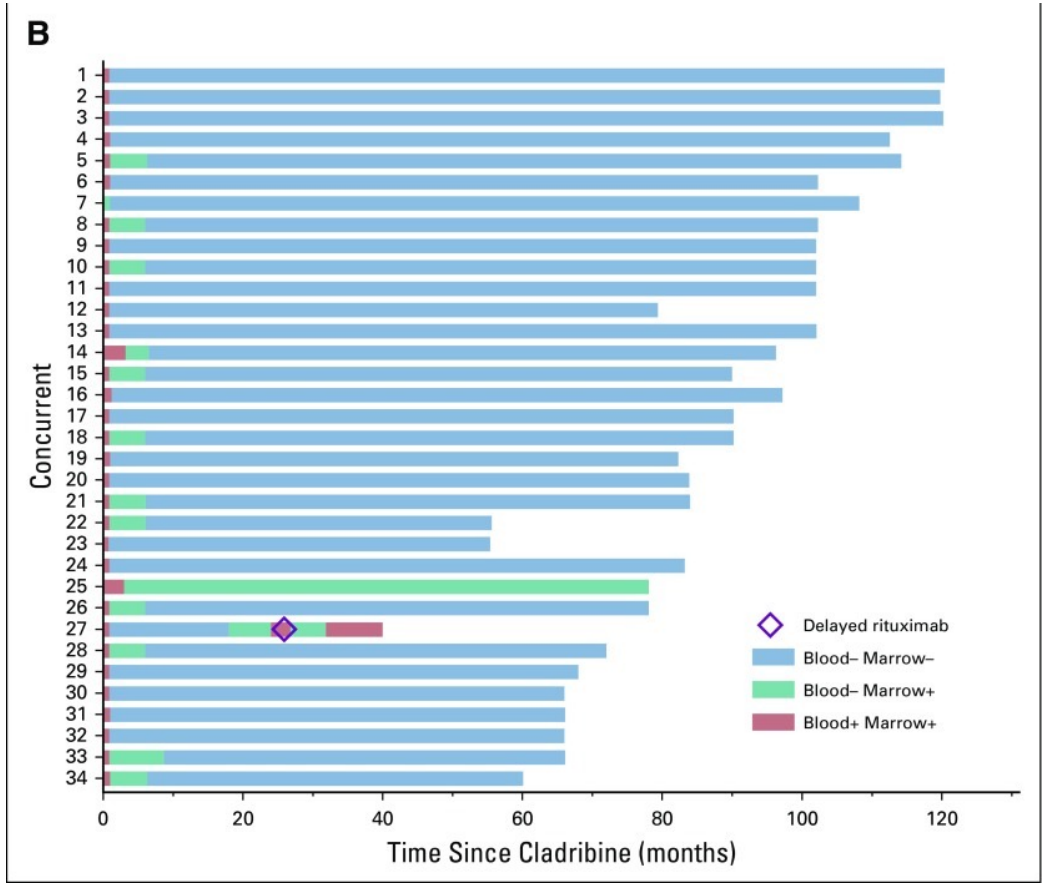
How to use these drugs?

How to use these drugs?

- Dose?
- Combinations?
- For how long?
- What are we aiming for?

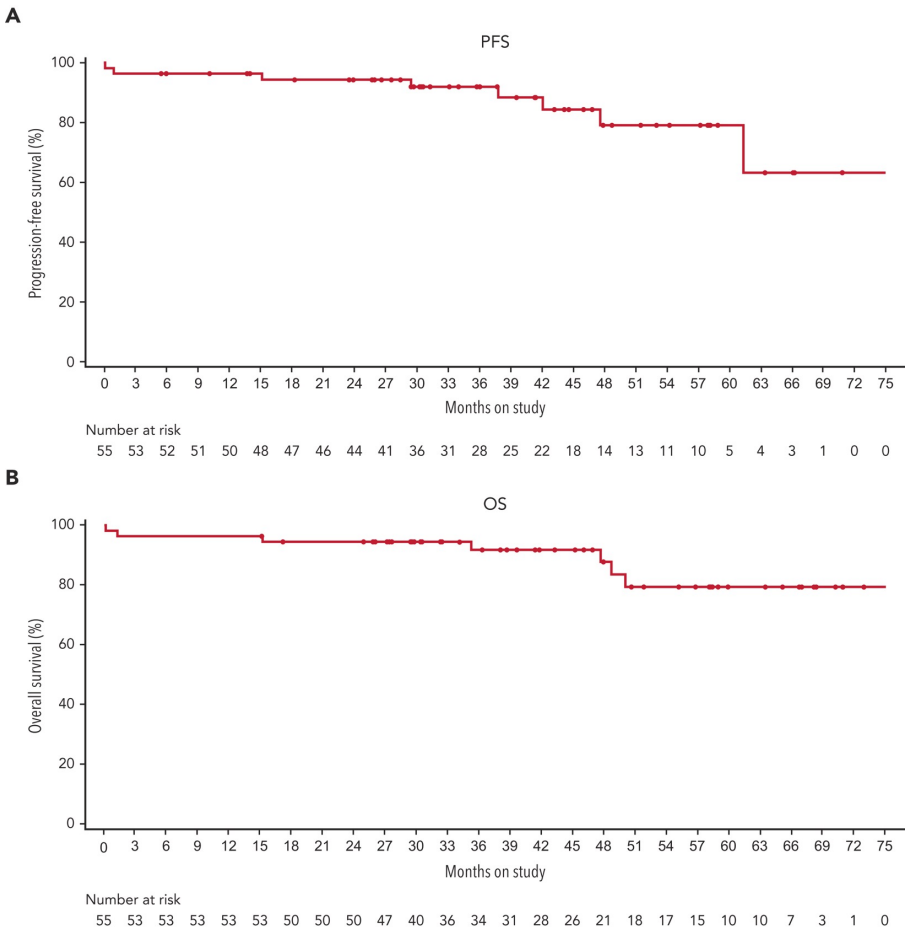
Example combinations:
Rituximab and purine analogues





Chihara et al J Clin Oncol. 2020 May 10; 38(14): 1527–1538.

Example combination: Dabrafenib and trametinib



Side effects (adverse events)

Fatigue
Chills
Fevers
Nausea
Rashes
Raised glucose
Skin cancers 7%

Subbiah et al Nat Med. 2023; 29(5): 1103–1112
Kreitman et al Blood (2023) 141 (9): 996–1006

New therapies on the horizon?

- New ways to target old targets? E.g. BTK enzyme
- New targets? E.g. BCL2 (venetoclax); ROR1
- Immunotherapies? Bispecifics or CAR-T, harnessing T cell power

Treat the person not the disease

Holistic management of patients

- Infection risk
- Psychological support
- Signpost to helpful groups/charities/ support networks