Allo Transplant for Follicular Lymphoma

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Disclosures

- I will discuss off-label use
- Conflicts of interest
  - Consultancy

    BMS, Merck, Pfizer, Infinity
  - Research funding (institutional)

    BMS, Merck, Pfizer, Affimed, Sequenta, Otsuka, Adaptive/Sequenta, Sigma Tau

Introduction

- A paradox
  - Allo is a cure for an incurable disease…
  - Yet not often used

Introduction

- A paradox
- 11.5 minutes to propose a solution

Introduction

- A paradox
- 11.4 minutes to propose a solution
  - Why? *Molto facile*

Introduction

- A paradox
- 11.3 minutes to propose a solution
  - Why? *Molto facile*
  - Who/How? *Facile*

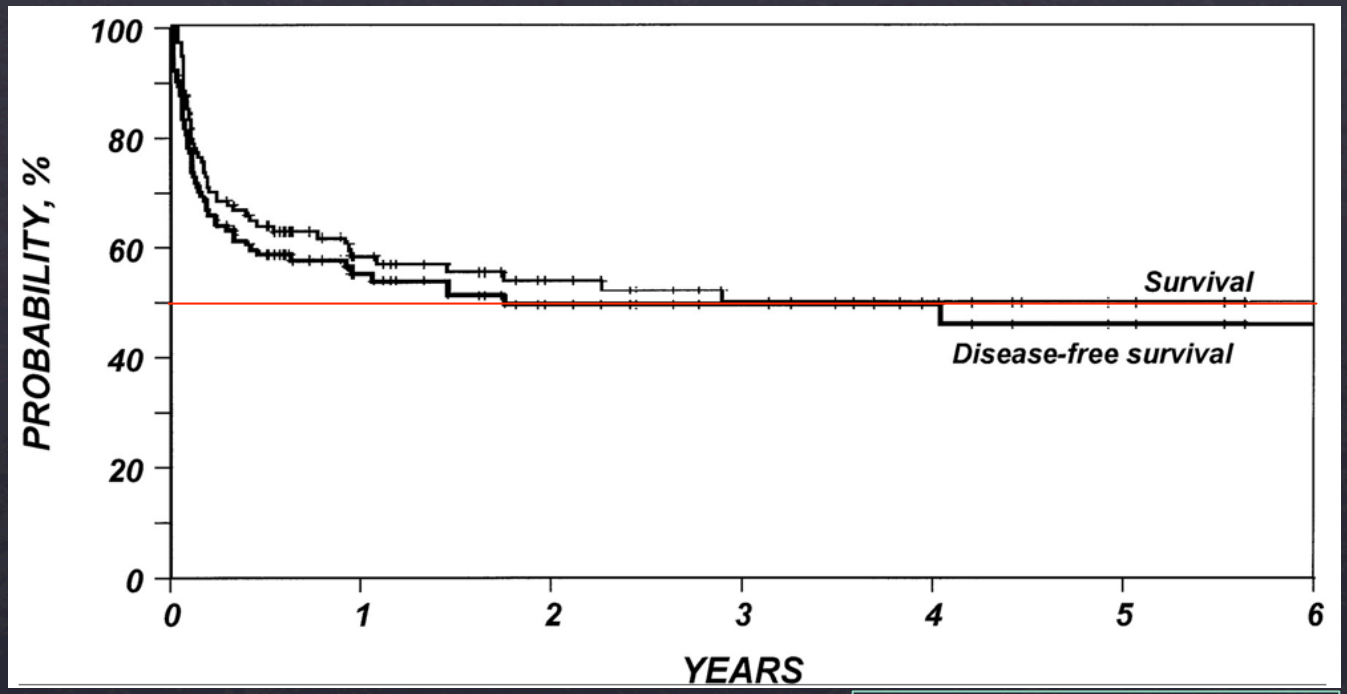
Introduction

- A paradox
- 11.2 minutes to propose a solution
  - Why? *Molto facile*
  - Who/How? *Facile*
  - When? *Impossibile*

Why Allo in FL?

Why Allo in FL?

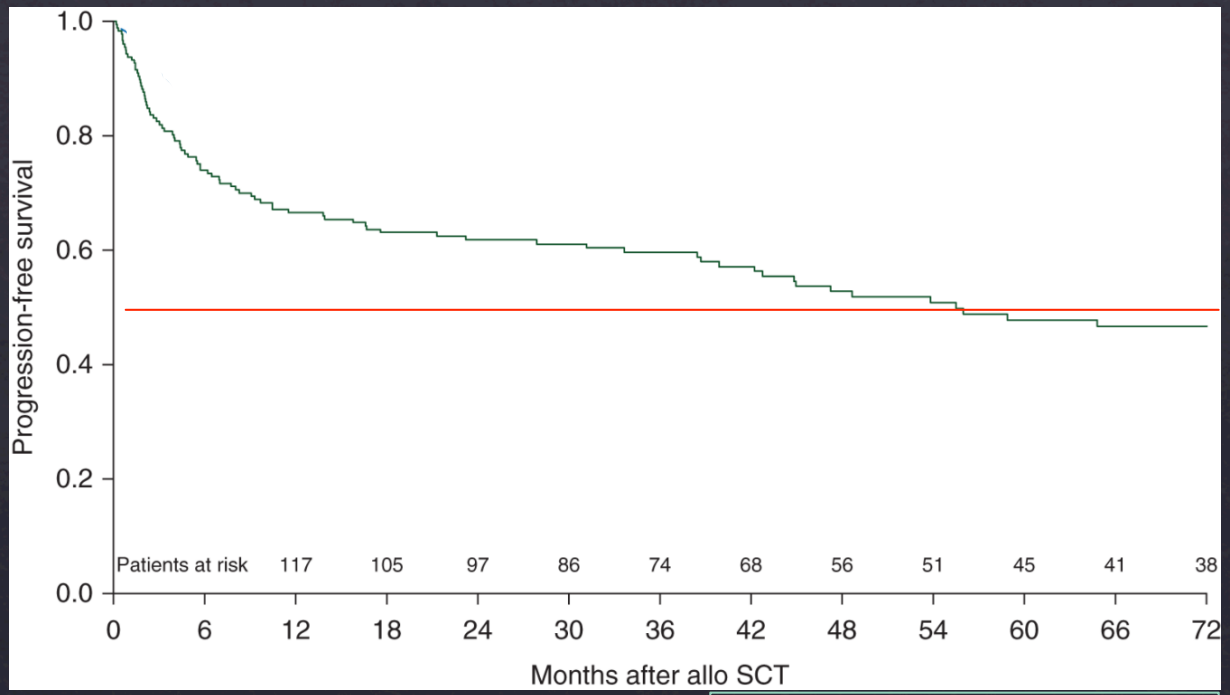
- A cure for the incurable
  - IBMTR 113 pts (41 with FL): 5y DFS ~50%



Van Besien, Blood 1998

Why Allo in FL?

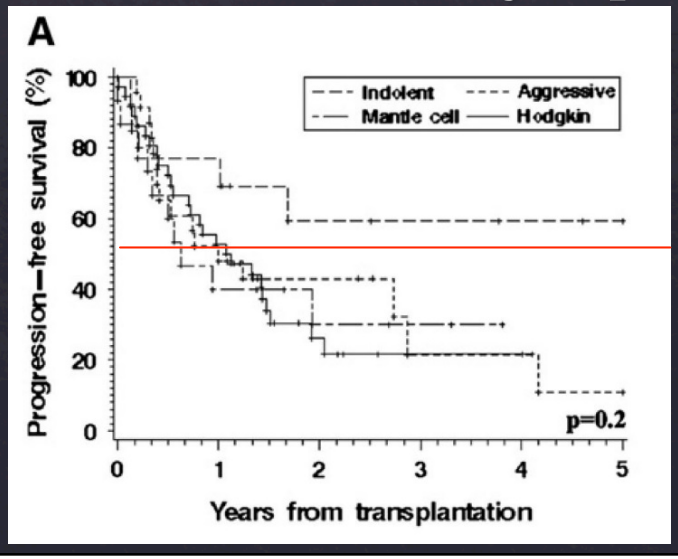
- A cure for the incurable
  - IBMTR 113 pts (41 with FL)
  - EBMTR 183 pts (RIC): 5y PFS ~50%



Robinson, Ann Onc 2016

Why Allo in FL?

- A cure for the incurable
  - IBMTR 113 pts (41 with FL)
  - EBMTR 183 pts: 5y PFS ~50%
  - And many many others in between
    - FL best outcome of all lymphomas with allo



Armand, BBMT 2008

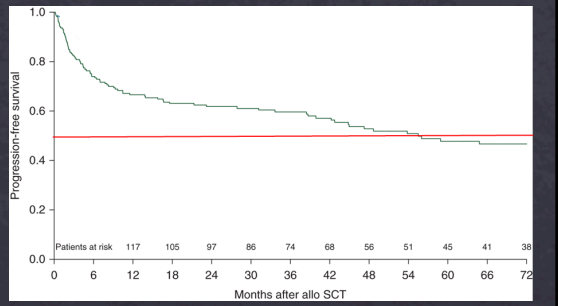
Why Allo in FL?

- A cure for the incurable
- Our first benchmark
  - ~½ allo pts are disease-free @5y w/ plateau

Who and How?

Who and How?

- Who?
  - Curative potential exists in RIC



Who and How?

- Who?
  - Curative potential exists in RIC
  - Opens the window wide
    - Age to late 70s
    - Mild-moderate comorbid conditions tolerable
    - Less selection bias than clinical trial?

Brunner, BBMT 2013

Who and How?

- Who?
  - Curative potential exists in RIC
  - Opens the window wide
  - The question of disease status
    - Easy: transplant in remission (better outcome)

Van Besien, Blood 1998
Robinson, Ann Onc 2016
Rezvani, JCO 2007
Hari, BBMT 2008
Delgado, Leukemia 2010
Pinana, Haematologica 2010
Etc…

Who and How?

- Who?
  - Curative potential exists in RIC
  - Opens the window wide
  - The question of disease status
    - Easy: transplant in remission
    - Haunting: transplant with SD/PD

Who and How?

- Who?
  - Curative potential exists in RIC
  - Opens the window wide
  - The question of disease status
  - Bottom line: many candidates…

Who and How?

- Who?
- How?
  - MAC vs RIC
    - No prospective study in lymphoma
    - Retrospective series
      - MAC higher NRM/lower relapse
      - Generally roughly similar PFS/OS

Rodriguez, BBMT 2006
Hari, BBMT 2008
Avivi, BJH 2009

Who and How?

- Who?
- How?
  - MAC vs RIC
  - Rituximab
    - Rationale
      - May improve disease and GVHD control
      - When is R not helpful in FL?...

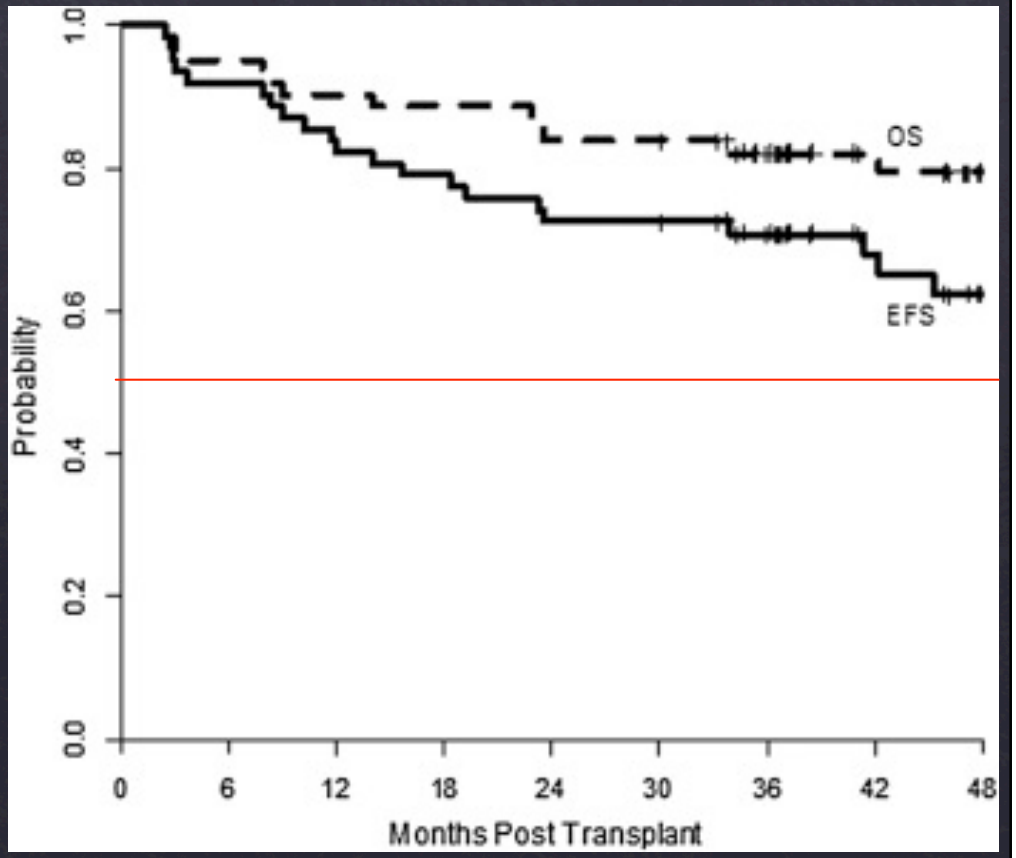
Who and How?

- Who?
- How?
  - MAC vs RIC
  - Rituximab
    - Rationale
    - MDACC experience
      - 47 pts
      - 5y PFS 83%

Khouri Blood 2008

Who and How?

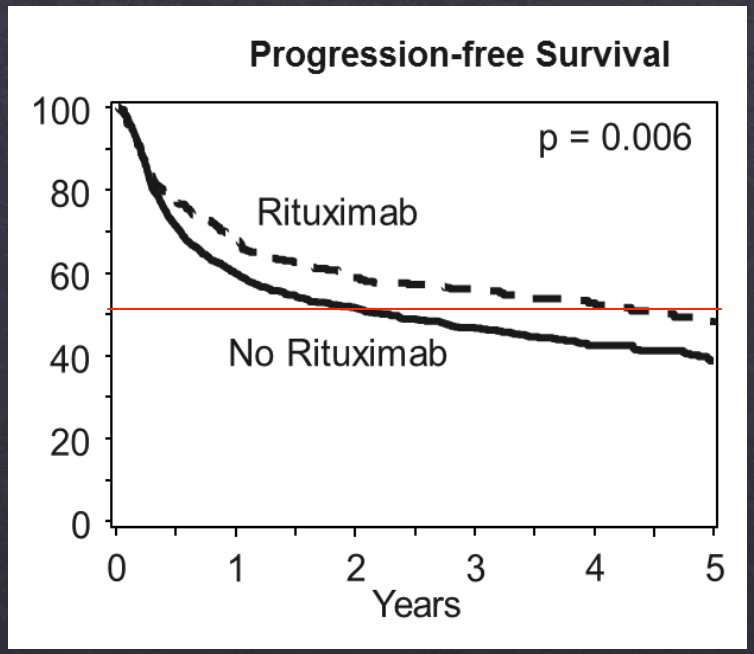
- Who?
- How?
  - MAC vs RIC
  - Rituximab
    - Rationale
    - MDACC experience
    - CTN study
      - 65 pts
      - 3y PFS 71%



Laport BBMT 2016

Who and How?

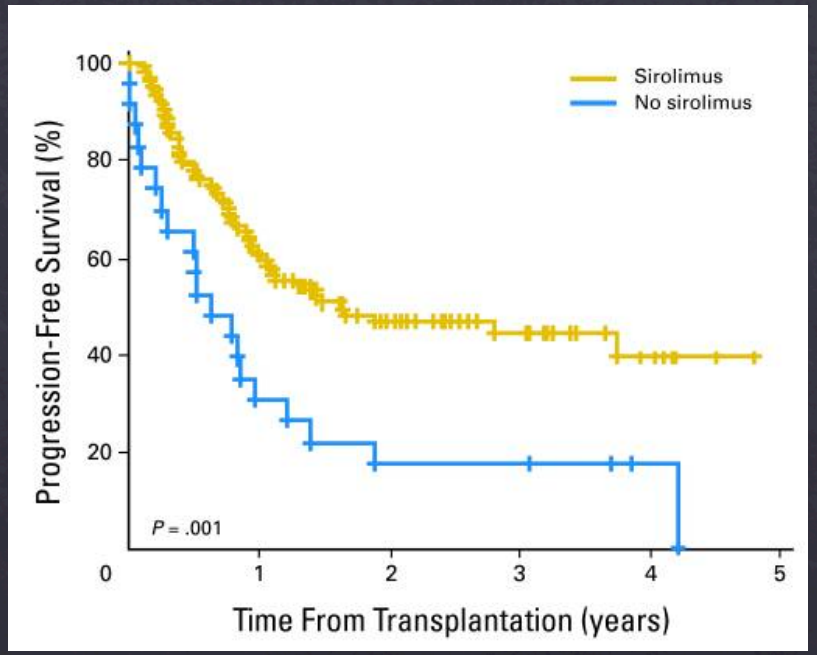
- Who?
- How?
  - MAC vs RIC
  - Rituximab
    - CIBMTR study
      - 1401 B-NHL pts (410 FL) all RIC
      - 3y PFS 56% with R vs 47% without (p=0.006)
      - 3y OS 64% with R vs 56% without (p=0.01)



Epperla, submitted

Who and How?

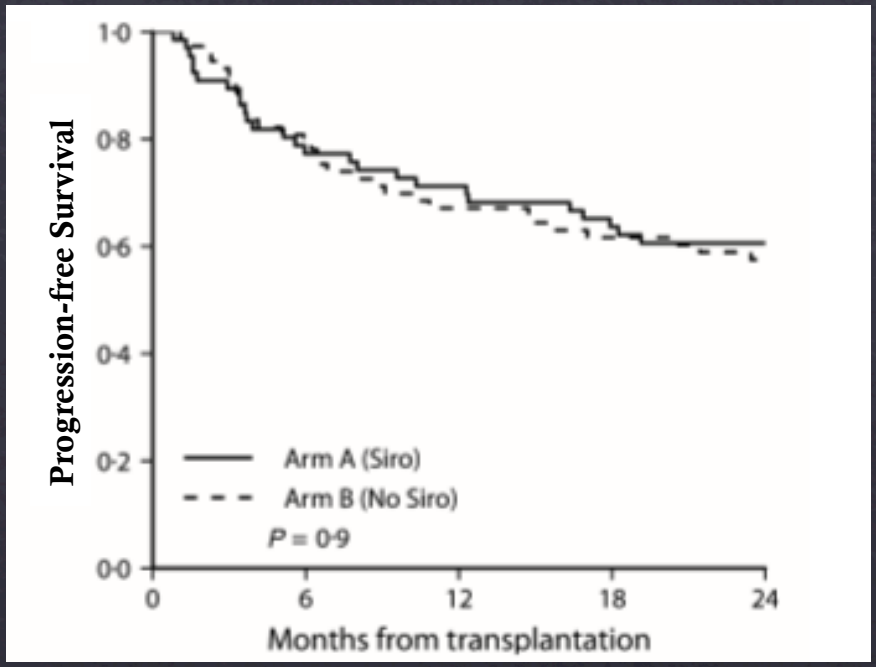
- Who?
- How?
  - MAC vs RIC
  - Rituximab
  - Sirolimus
    - Another possible double agent
    - PFS/OS benefit in retrospective lymphoma study
      - Benefit limited to RIC patients



Armand, JCO 2008

Who and How?

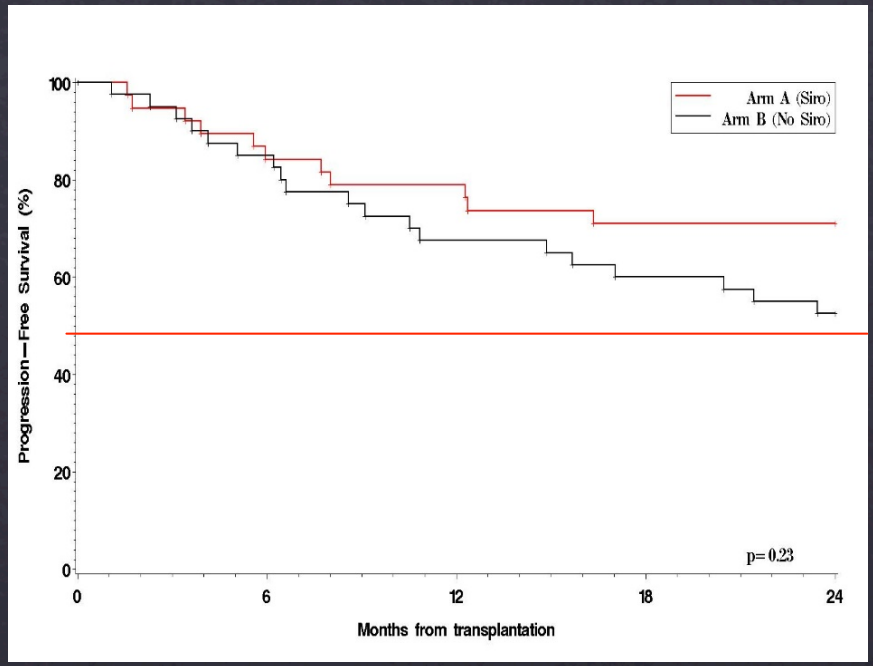
- Who?
- How?
  - MAC vs RIC
  - Rituximab
  - Sirolimus
    - Phase 3 trial Tac/Mtx vs Tac/Siro/Mtx
    - No difference overall



Armand, BJH 2016

Who and How?

- Who?
- How?
  - MAC vs RIC
  - Rituximab
  - Sirolimus
    - Phase 3 trial Tac/Mtx vs Tac/Siro/Mtx
    - No difference overall
    - Trend for benefit in indolent NHL/HL



Armand, BJH 2016

Who and How?

- Who?
- How?
  - MAC vs RIC
  - Rituximab
  - Sirolimus
    - Phase 3 trial Tac/Mtx vs Tac/Siro/Mtx
    - CIBMTR Rituximab study
      - HR for PFS sirolimus 0.6, p=0.003
      - HR for OS 0.6, p=0.002

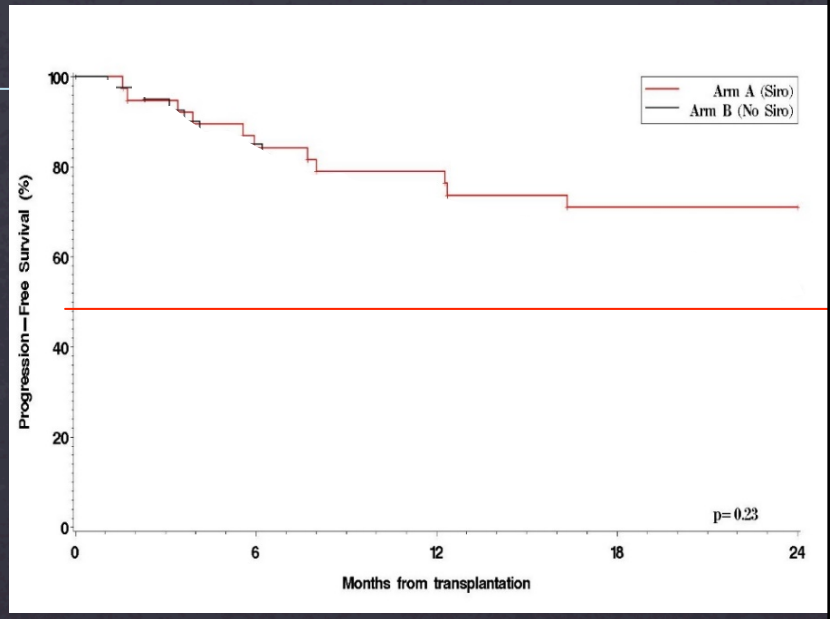
Epperla, submitted

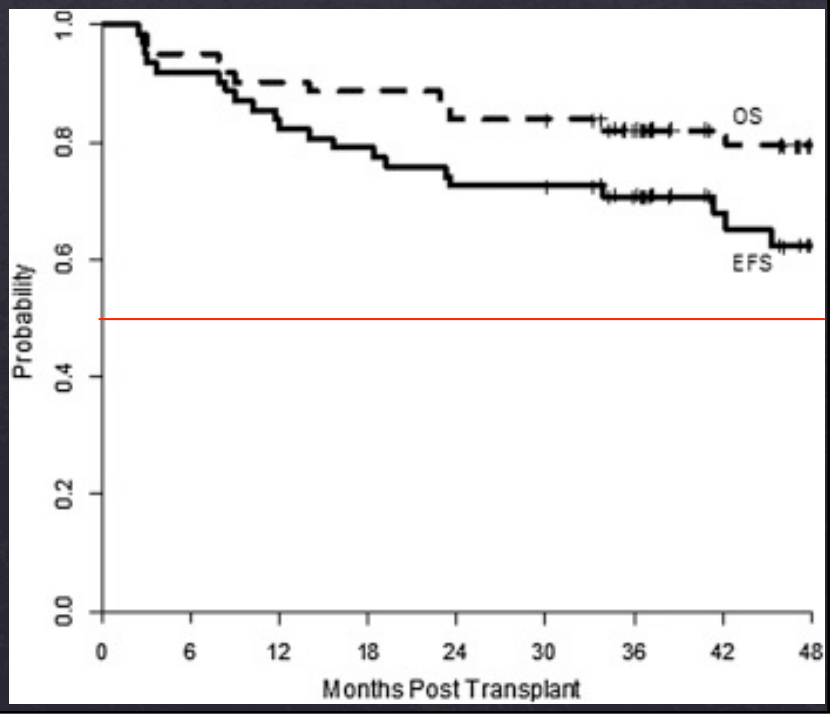
Who and How?

- Who?
- How?
  - The bottom line
    - RIC allo in most
    - Rituximab-containing conditioning
    - Tac/Siro/Mtx for GVHD prophylaxis

Who and How?

- Who?
- How?
  - The bottom line
  - A modern benchmark
    - Excellent outcomes…
      - 4y PFS ~60%
      - 4y OS ~80%
    - NRM 10-15%





When?

When?

- Herein is the problem
  - A curative but toxic procedure…
  - In a disease with a lot of options

When?

- Herein is the problem
- Randomized data easy to summarize
  - CTN phase 3 “genetic rand” trial
    - RIC allo vs auto
    - (Remember auto OS benefit in CUP)
    - FCR conditioning
    - 30 pts (closed for accrual)
    - At median f/u 3y, PFS allo 86% vs 63%

Schouten JCO 2003
Tomblyn, BBMT 2011

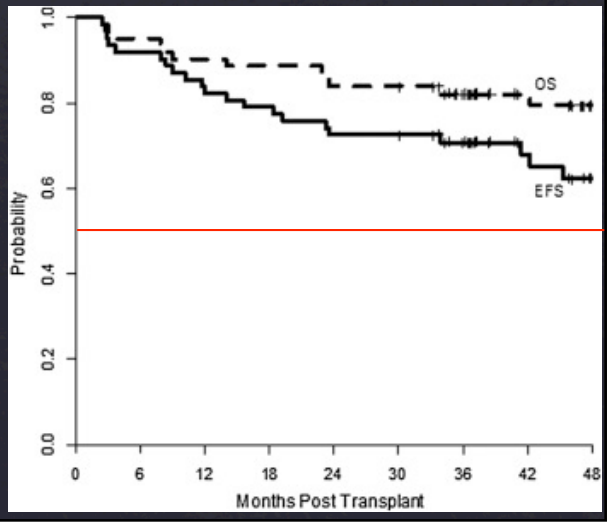
When?

- Herein is the problem
- Randomized data easy to summarize
- Crossing the commitment threshold

When?

- Herein is the problem
- Randomized data easy to summarize
- Crossing the commitment threshold
  - Comparison metrics
    - Need to compare allo PFS to drug X DOR
    - While using OS as final arbiter

(drug effectiveness + state of field)



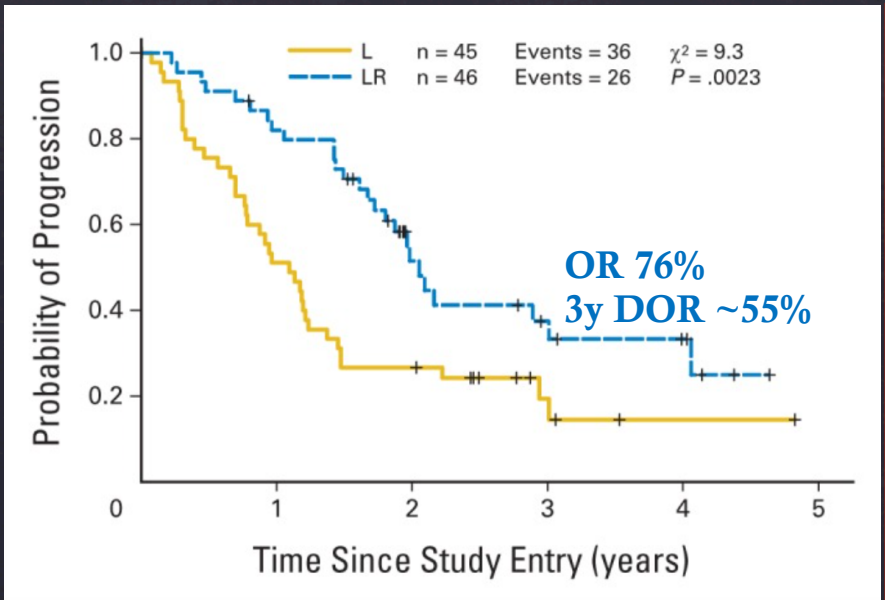
When?

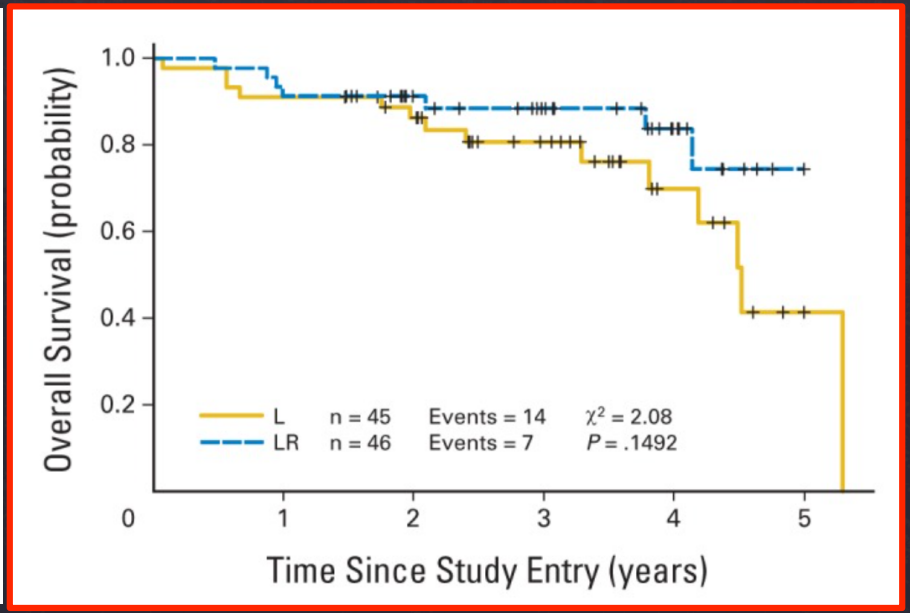
- Herein is the problem
- Randomized data easy to summarize
- Crossing the commitment threshold
  - Consider R+lenalidomide
    - Phase 2, 46 pts on R/len arm

Leonard, JCO 2015

When?

- Herein is the problem
- Randomized data easy to summarize
- Crossing the commitment threshold
  - Consider R+lenalidomide





When?

- Herein is the problem
- Randomized data easy to summarize
- Crossing the commitment threshold
  - Consider R+lenalidomide
    - Early patients?
    - Good enough salvage options?

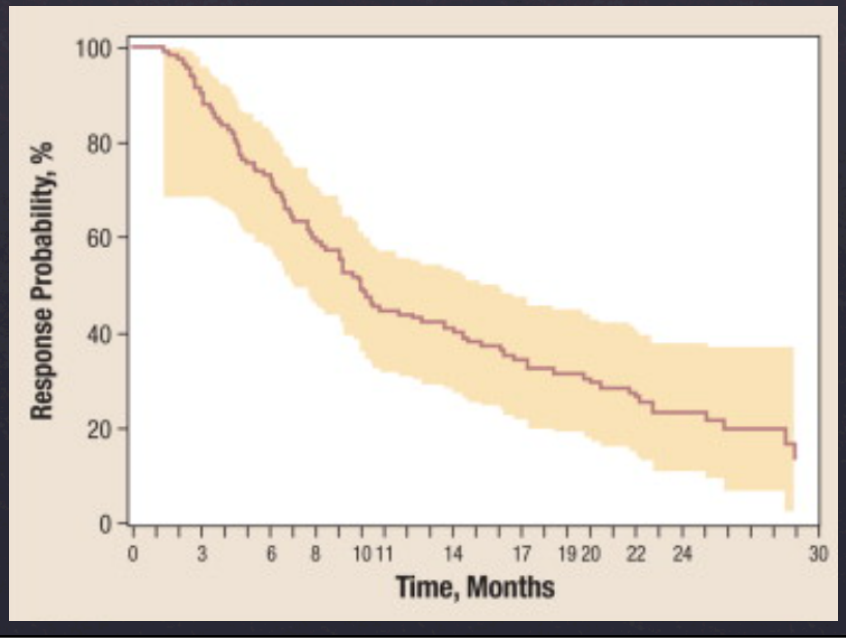
When?

- Herein is the problem
- Randomized data easy to summarize
- Crossing the commitment threshold
  - Consider (salvage) bendamustine
    - Pooled ph2 trial analysis
    - 161 pts
    - Median 2 prior

Cheson, Clin Lymph Myeloma Leuk 2010

When?

- Herein is the problem
- Randomized data easy to summarize
- Crossing the commitment threshold
  - Consider (salvage) bendamustine



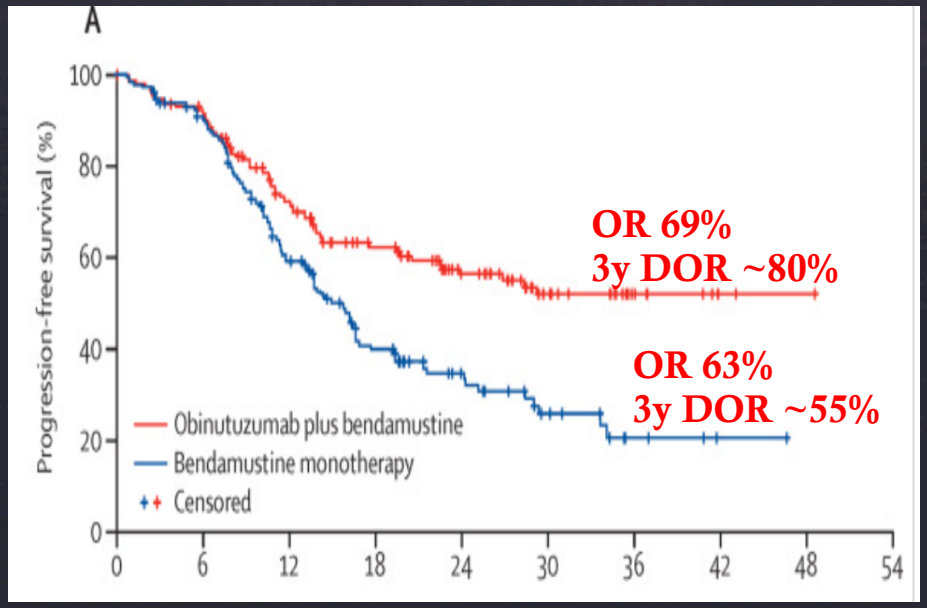
When?

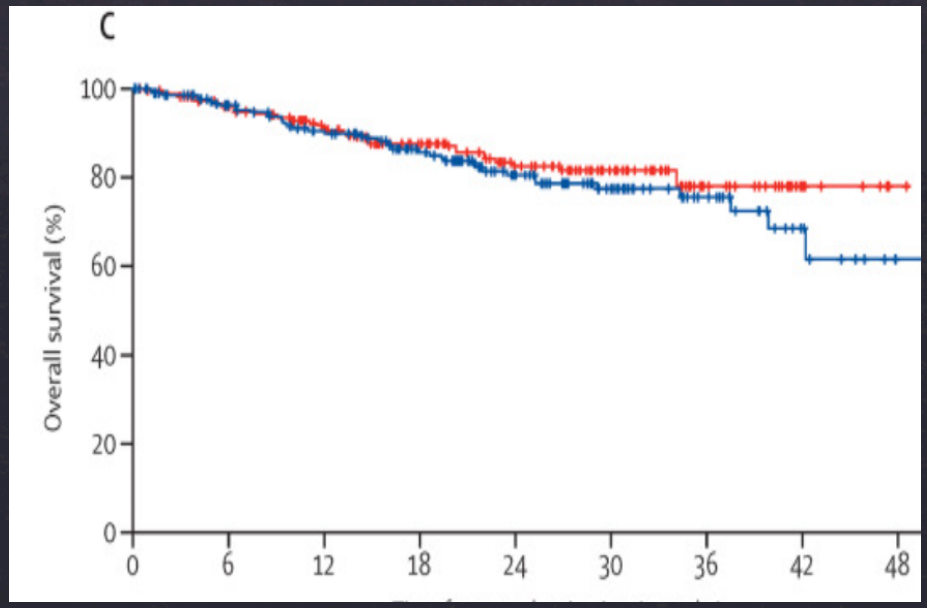
- Herein is the problem
- Randomized data easy to summarize
- Crossing the commitment threshold
  - Consider (salvage) bendamustine
    - 155 pts FL treated O-benda on GADOLIN
    - Median 2 prior

Sehn, Lancet Onc 2016

When?

- Herein is the problem
- Randomized data easy to summarize
- Crossing the commitment threshold
  - Consider (salvage) bendamustine





When?

- Herein is the problem
- Randomized data easy to summarize
- Crossing the commitment threshold
  - Consider (salvage) bendamustine
    - Allo may rival benda by itself
    - Even relatively early in course…
    - In combination may be superior

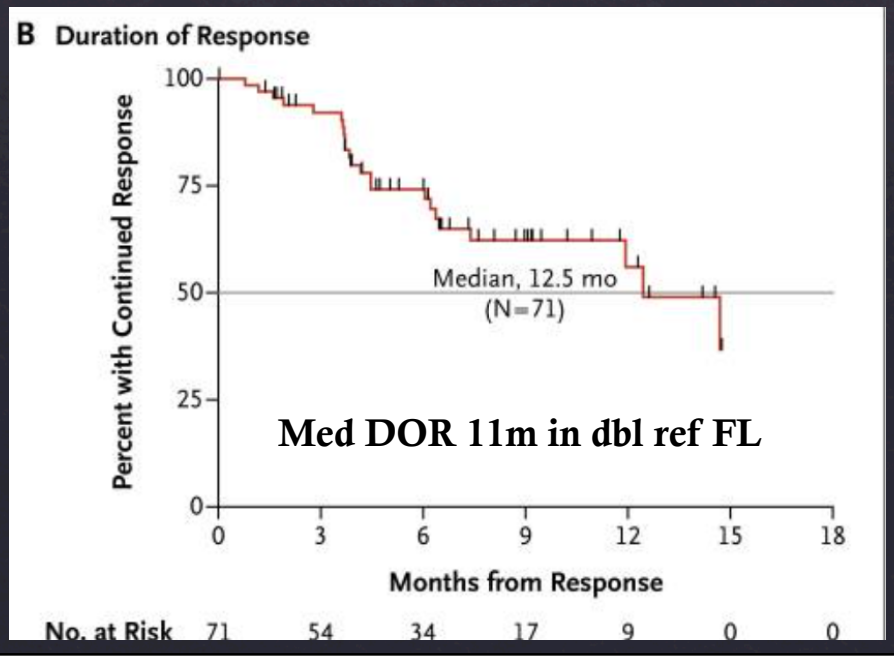
When?

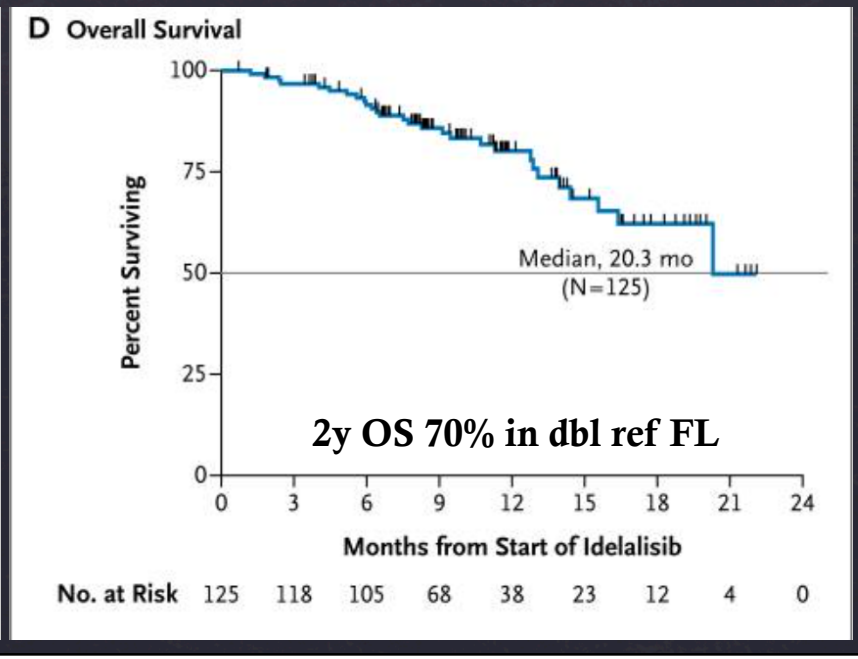
- Herein is the problem
- Randomized data easy to summarize
- Crossing the commitment threshold
  - Consider idelalisib
    - 125 pts phase 2 (72 FL)
    - Median 4 prior

Gopal, NEJM 2014
Salles Haematologica 2016

When?

- Herein is the problem
- Randomized data easy to summarize
- Crossing the commitment threshold
  - Consider idelalisib





When?

- Herein is the problem
- Randomized data easy to summarize
- Crossing the commitment threshold
  - Consider idelalisib
    - Strong argument for allo (in dbl ref)…

Conclusion

- Why?
  - Effective curative therapy
- Who?
  - Many patients up to late 70s
- How?
  - RIC + R and sirolimus
- When?
  - Viable consideration after 3 lines, strong afterwards
  - Modulated by responsiveness: R-ref, alk-ref
  - Will depend on future of experimental therapies (CAR-T)

GRAZIE!