

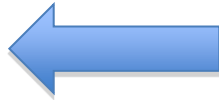
# Case #1

## Managing Treatment Options for Mantle Cell Lymphoma: When, For Whom, How Much?

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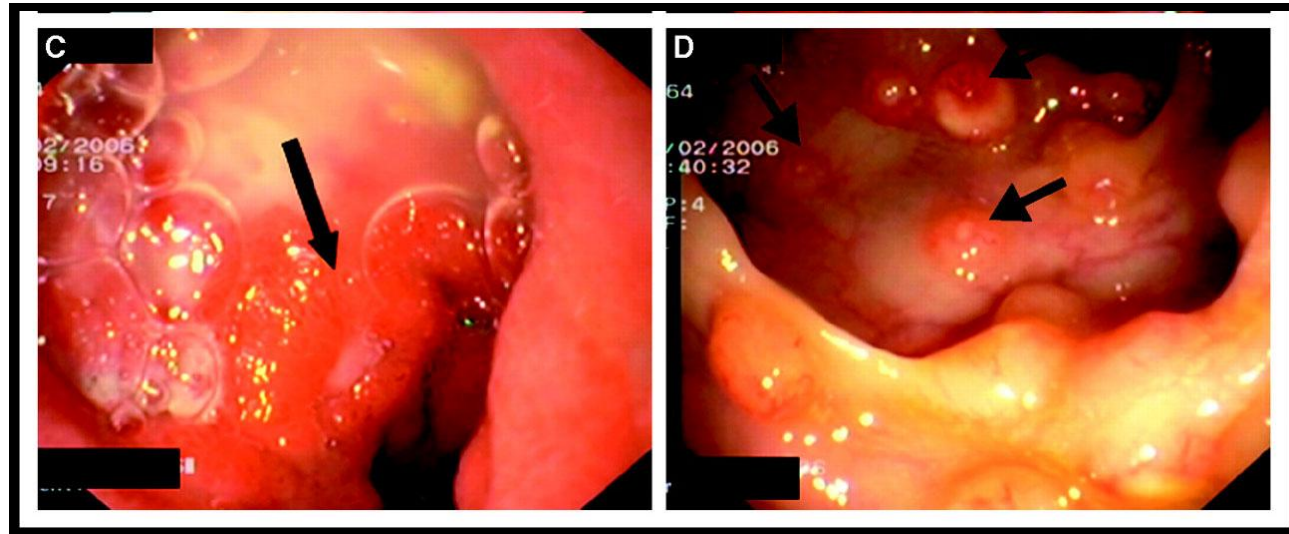
# Part I: Would you refer the patient for GI endoscopy prior to chemotherapy?

- Yes
- No



# Gastrointestinal location in MCL

- Clinically: Multiple lymphomatous polyposis
  - Abdominal pain
  - Diarrhea
  - Melena



- Seen in other lymphoma subtypes

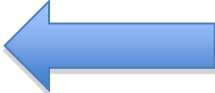
# Gastrointestinal location in MCL

- Clinically: symptomatic in 30% of MCL
  - Stomach, intestine, or colon
- Abnormal mucosa on endoscopy:
  - 38% in stomach
  - 54% in colon
- Histological infiltration by MCL
  - 77% in stomach and colon
- >90% with MCL histological infiltration

# **Part I: Would you refer the patient for GI endoscopy prior to chemotherapy?**

- Yes
  - If patient has clinical symptoms
- No
  - Without Gastrointestinal symptom
  - Assume that all patients had GI location
  - As blood, bone marrow and nodal locations

## Part II: What chemotherapy would you recommend?

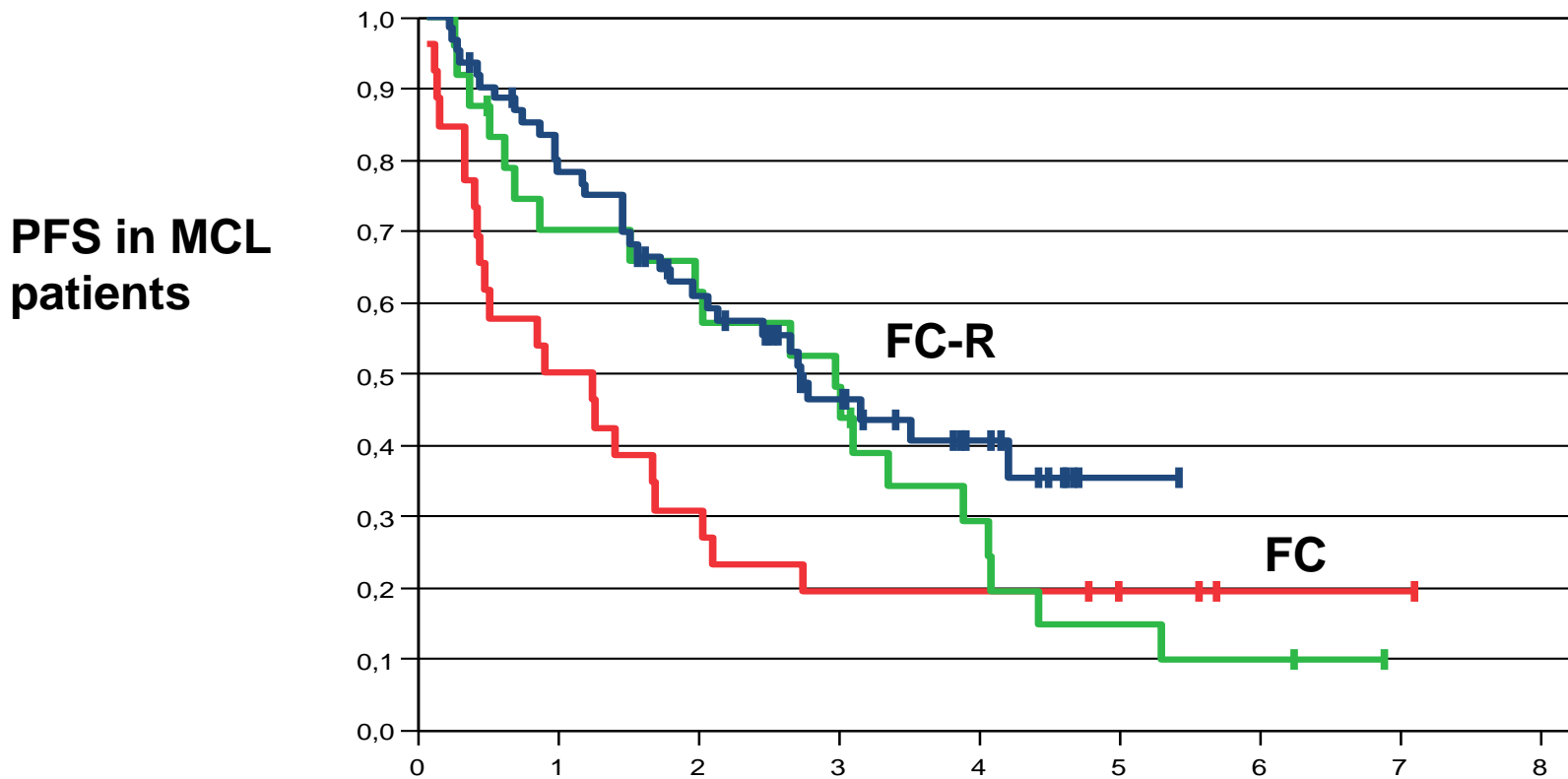
- CHOP + rituximab (Rituxan<sup>®</sup>/MabThera<sup>®</sup>)
- Intensive chemotherapy including MTX, high-dose Ara-C + rituximab
- Chemotherapy + rituximab followed by autologous stem cell transplant (SCT) 
- Chemotherapy + rituximab followed by matched sibling allogeneic SCT
- Bortezomib (Velcade<sup>®</sup>) on a clinical trial

# Standard Chemotherapy for MCL

- No standard at all
- Rituximab-chemotherapy is the treatment of choice
- Autologous transplant in first response is recommended by European Mantle Cell Consortium for young patients
- Which chemotherapy regimen?

# Rituximab-chemotherapy is the treatment of choice

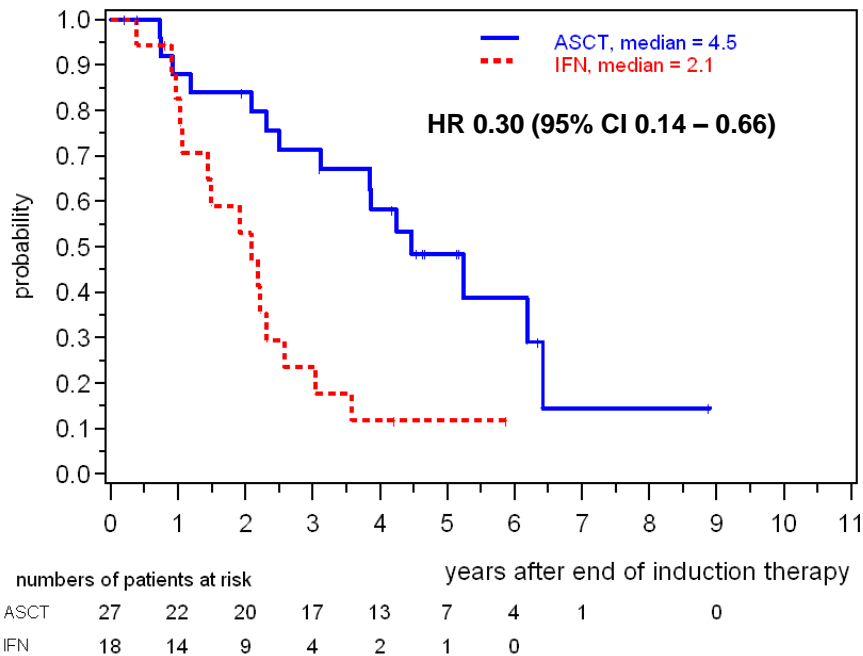
- Few randomized study



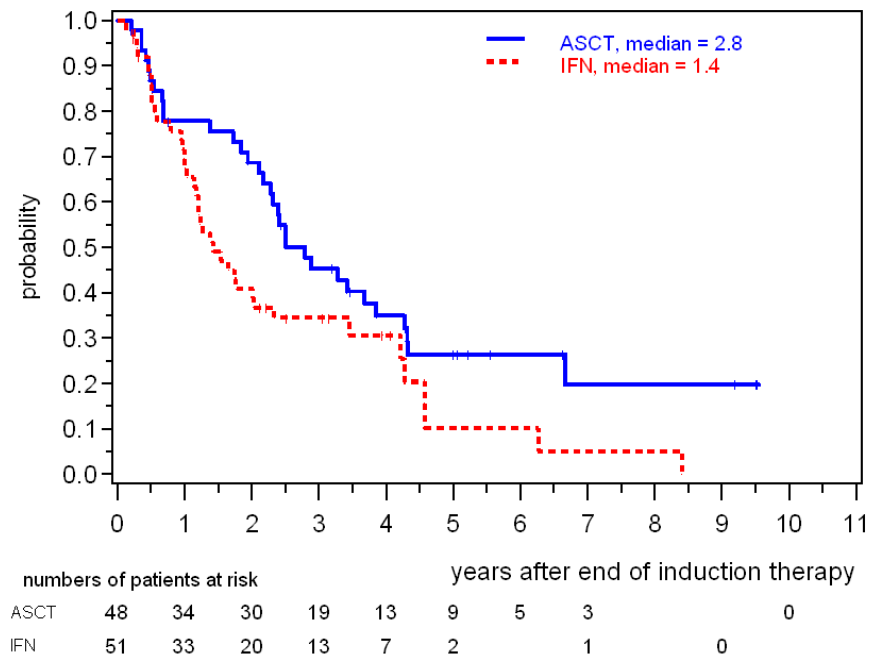
# Autologous transplant in first response is recommended for young patients

## Progression-free survival

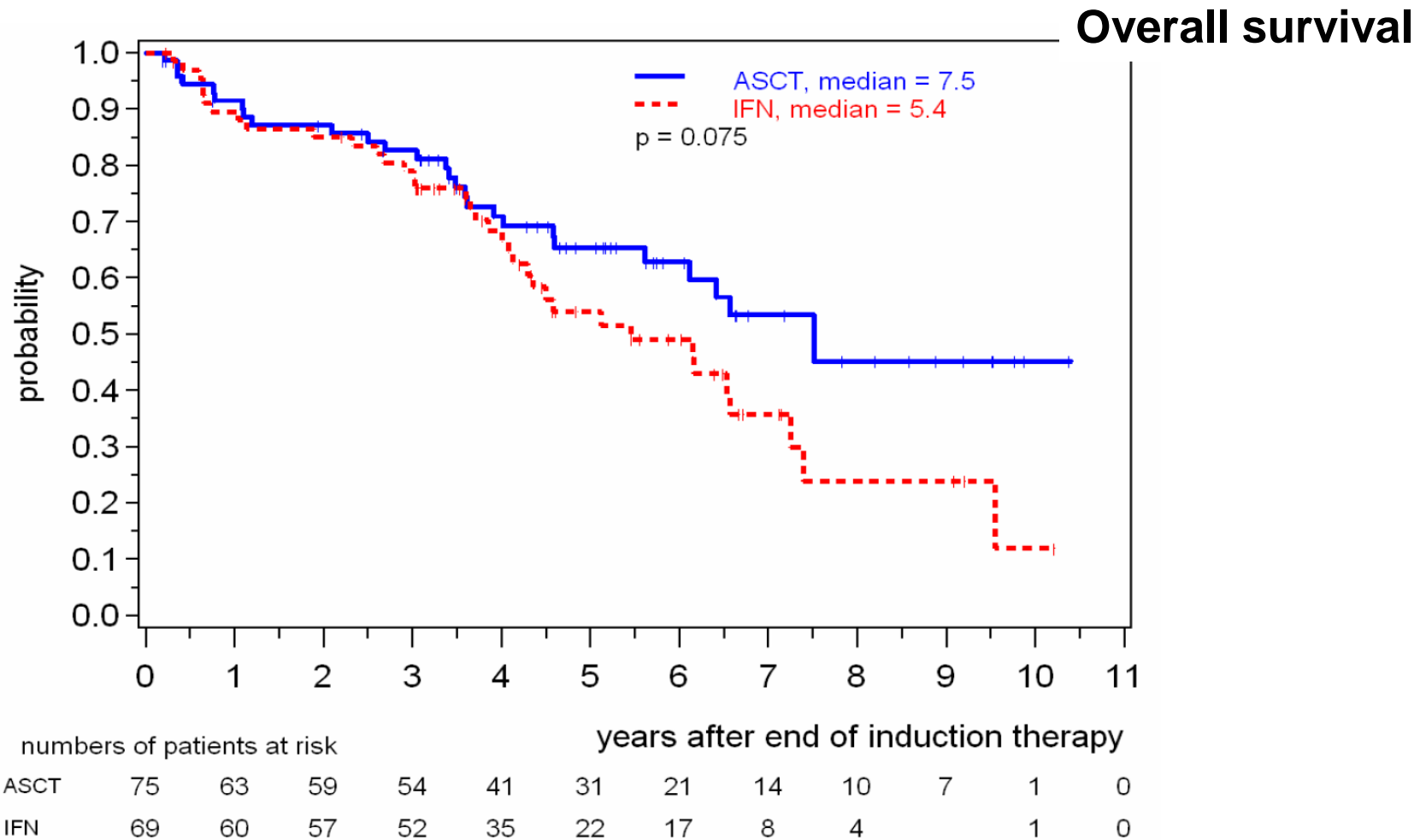
CR



PR



# Autologous transplant in first response is recommended for young patients



# Which chemotherapy regimen?

## **R-CHOP**

- Easy to administer
- No hematological toxicity
- Very few febrile neutropenia/infection
- No opportunistic infection
- Less active?

## **R-HyperCVAD/M-A**

- More complicated
- Hematological toxicity
- Infections
- Opportunistic infection
- More hospitalizations
- More active?

No direct comparison

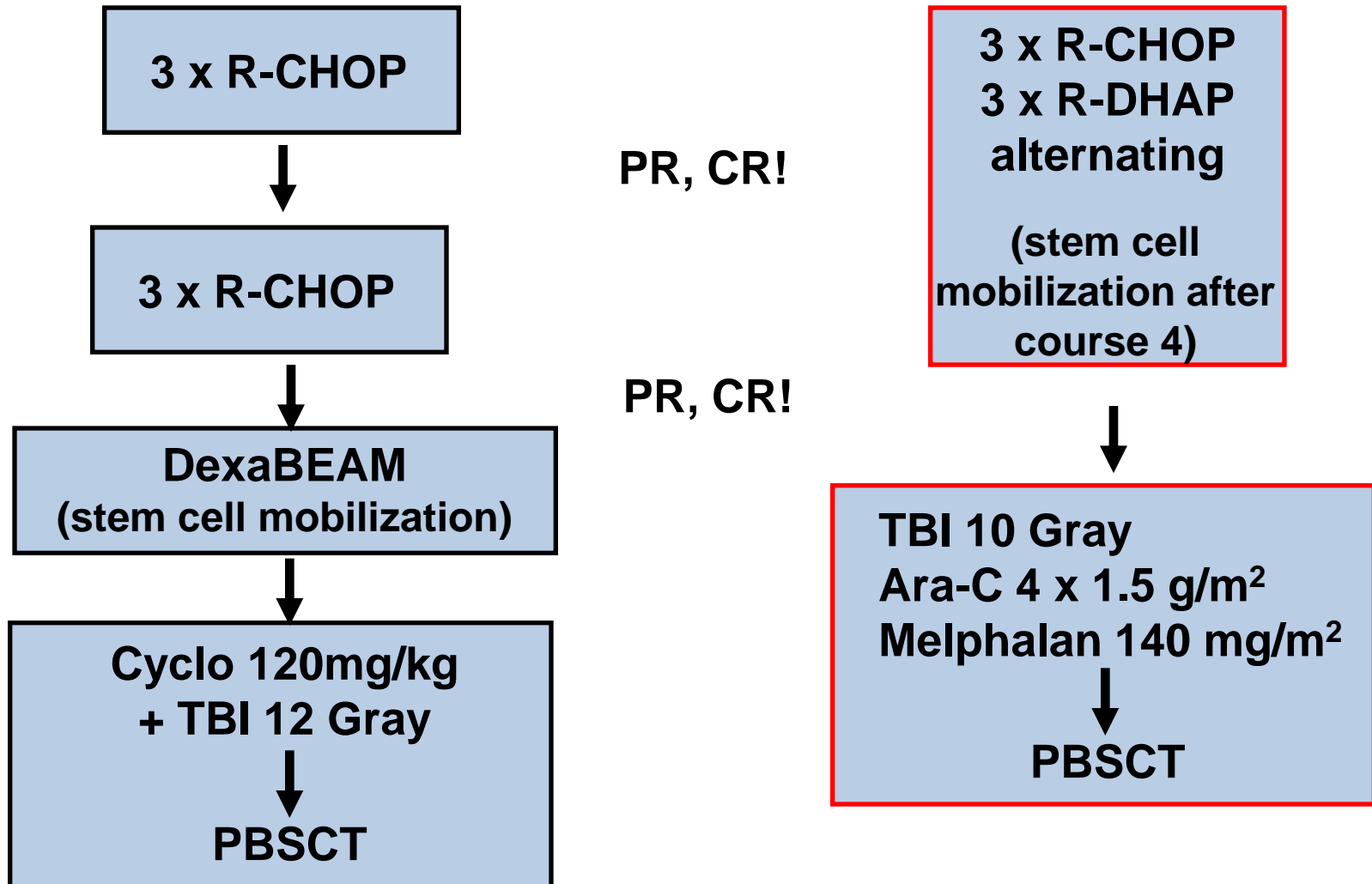
# Which chemotherapy regimen?

- R-CHOP
- R-HyperCVAD/M-A
- R-FC
- R-CHOP/R-DHAP
- Others

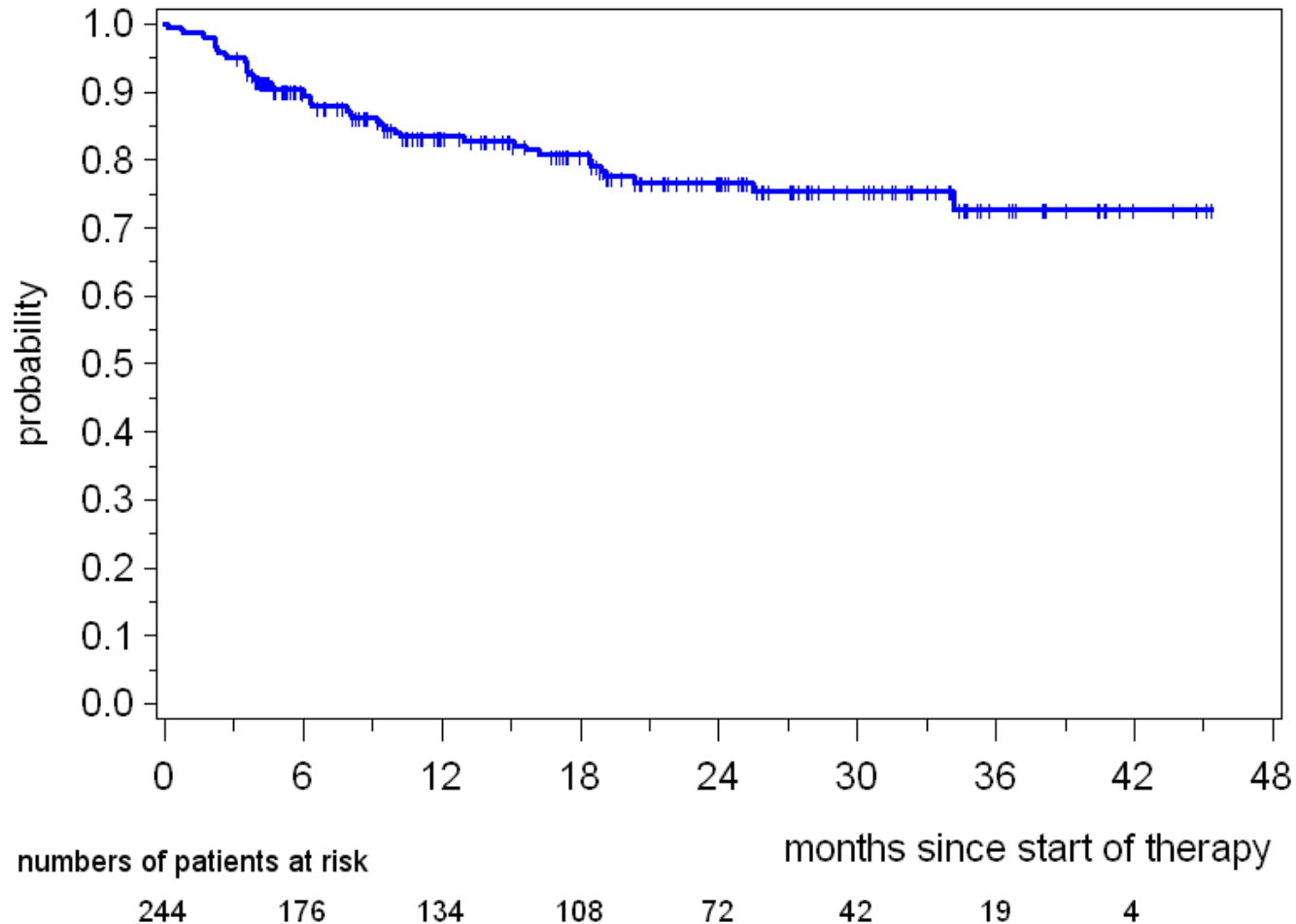
What is a good regimen?

A regimen well tolerated, easy to administer and active (allowing to reach a response and a transplant)

# *European MCL Network* patients <65 years

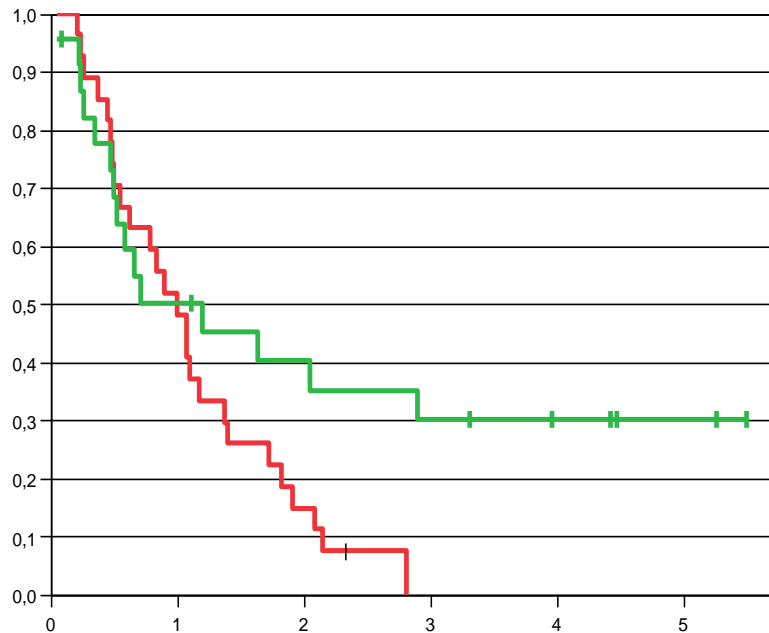


# European MCL Network: Young patients



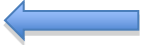
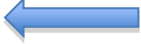

# First Line Treatment - Elderly

- R-FC was associated with a good response rate and a good safety
- Rituximab maintenance?



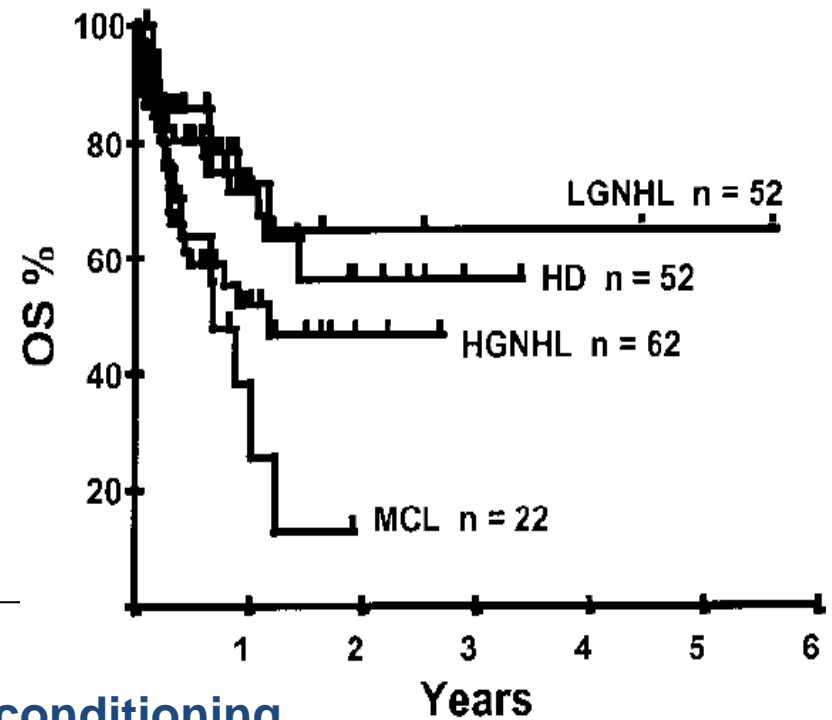
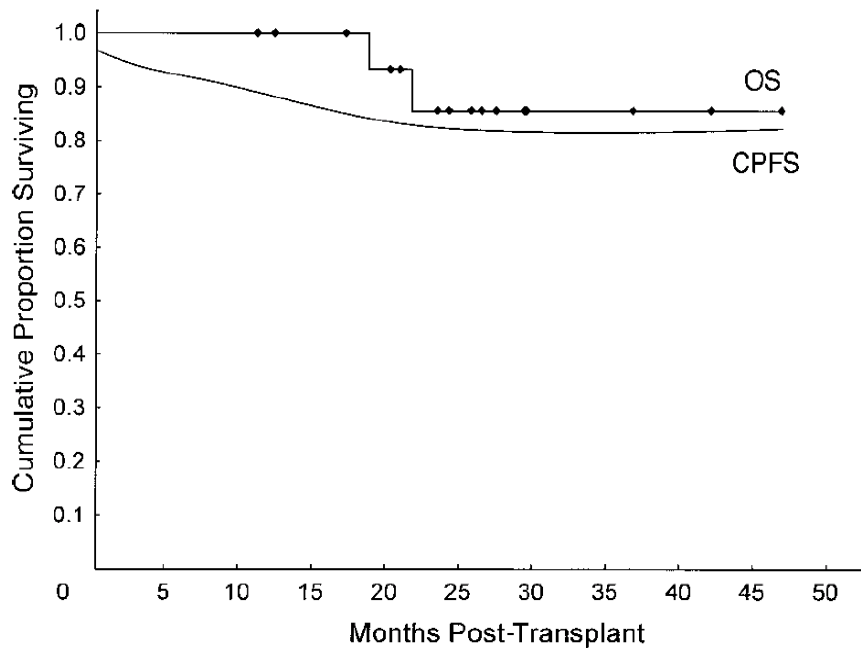
**Rituximab maintenance  
after R-FC in MCL**

# Part II: What would you now recommend?

- High-dose Ara-C ( $3\text{g}/\text{m}^2$  twice daily for three days) + mitoxantrone + rituximab
- Bortezomib
- MTX-based chemotherapy + rituximab
- R-DHAP (rituximab, dexamethasone, ara-C and cisplatin)
- Fludarabine-containing regimen (FCM) + rituximab 
- Rituximab monotherapy 
- Choice of radioimmunotherapy (Zevalin<sup>®</sup> or Bexxar<sup>®</sup>)
- Chemotherapy + rituximab followed by allogeneic SCT 
- Chemotherapy + rituximab followed by second autologous SCT
- Temsirolimus (Torisel<sup>®</sup>)  $175\text{ mg}/\text{m}^2$  weekly for three weeks followed by  $75\text{ mg}/\text{m}^2$  weekly
- Temsirolimus  $175\text{ mg}/\text{m}^2$  weekly for three weeks followed by  $25\text{ mg}/\text{m}^2$  weekly

# Treatment of relapse in a young patient?

- First choice: try to be curative = allogeneic transplant



Reduced conditioning

# Treatment of relapse in a young patient?

- Second choice: try to prolong survival = use non-toxic active regimen to get PR
  - Rituximab alone
  - Rituximab plus interferon & thalidomide
  - Rituximab plus chemotherapy (R-FC)
  - New drugs
    - Bortezomib
    - Lenalidomide
    - Temsirolimus

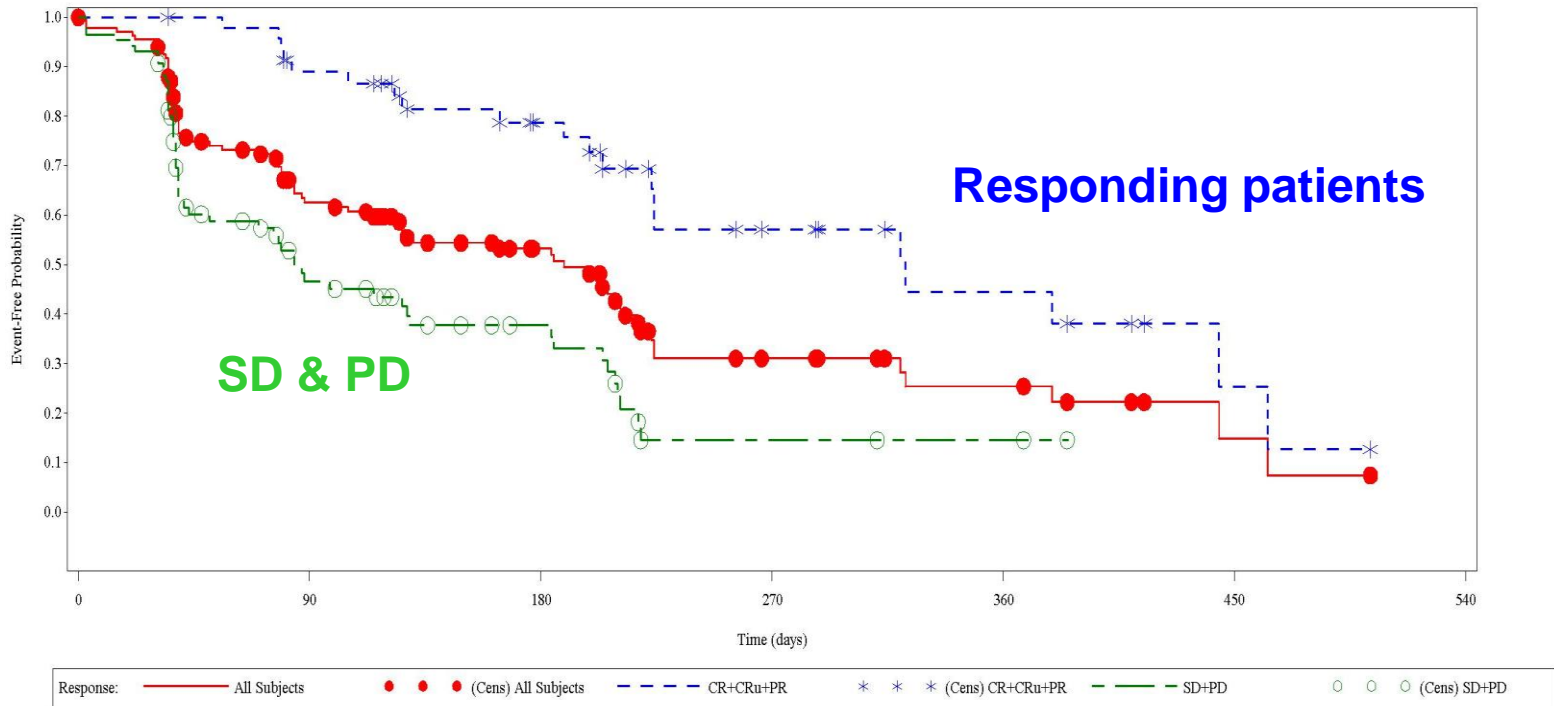
# Bortezomib in relapsed MCL (phase II studies)

Study	Design	Dose	n	CR/CRu	PR	ORR
O'Connor	d 1, 4, 8, 11 q 3 wks 8 cycles	1.5mg/m <sup>2</sup>	37	3/2 (13%)	10 (27%)	40%
Goy	Same 6 cycles	1.5mg/m <sup>2</sup>	29	6 (21%)	6 (21%)	41%
Strauss Lister	Same 6 cycles	1.3mg/m <sup>2</sup>	24	1 (4%)	6 (25%)	29%
Belch	Same 6 cycles	1.3mg/m <sup>2</sup>	13 untreated 15 treated	0 1	6 6	46% 47%
Goy	Same 17 cycles	1.3mg/m <sup>2</sup>	152 treated	8%	21%	33%

1. O'Connor OA, et al. *Ann Oncol.* 2005;16: Abstract 096. 2. Goy A, et al. *J Clin Oncol.* 2005;23(4):667-675. 3. Goy AH, et al. *Proc Am Soc Clin Oncol.* 2003;22: Abstract 229. 4. Strauss SJ, et al. *J Clin Oncol.* 2006;24(13):2105-2112. 5. Belch A, et al. *Blood.* 2004;104: Abstract 608. 6. Goy A, et al. *J Clin Oncol.* 2006;24(18S): Abstract 7512. 7. Fisher RI, et al. *J Clin Oncol.* 2006;24(30):4867-4874.

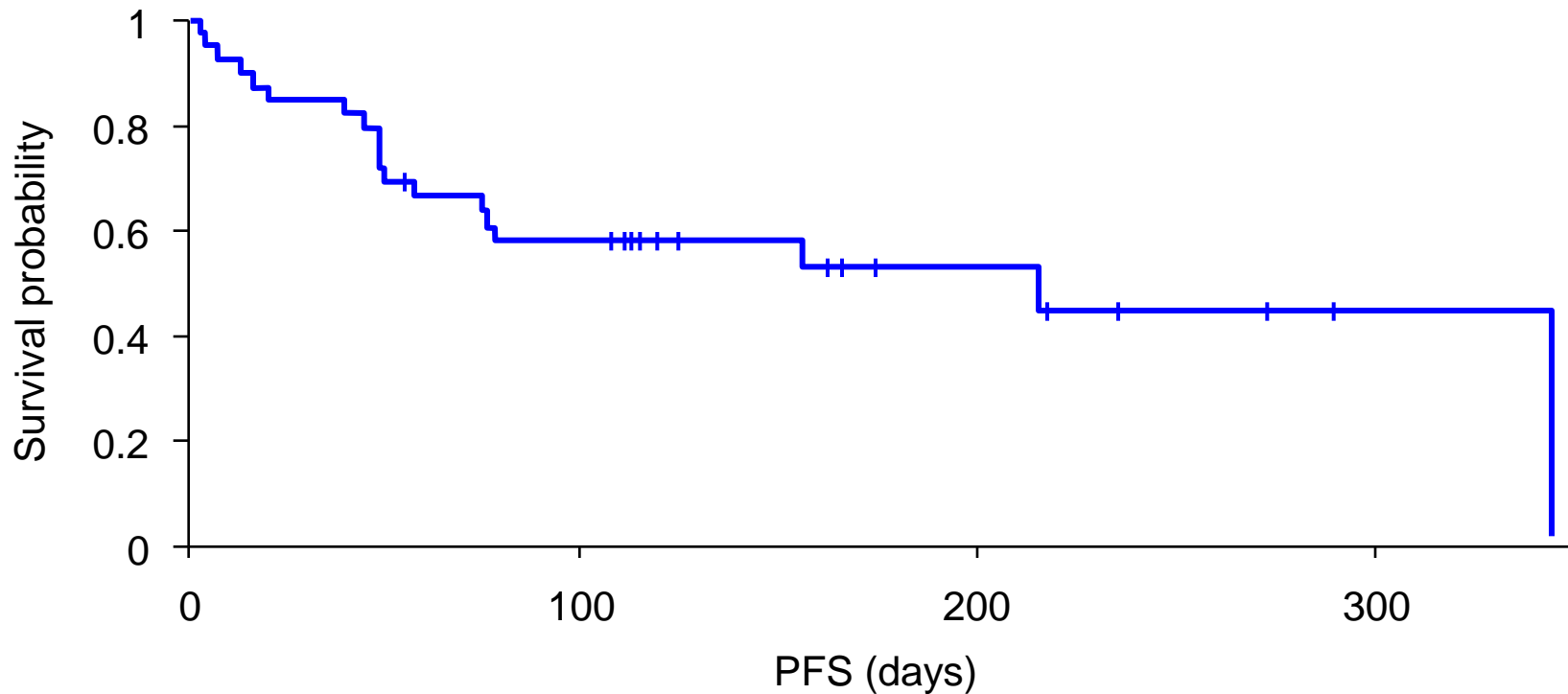
# Bortezomib in MCL

Progression-free survival (red)  
responders (blue), non-responders (green)



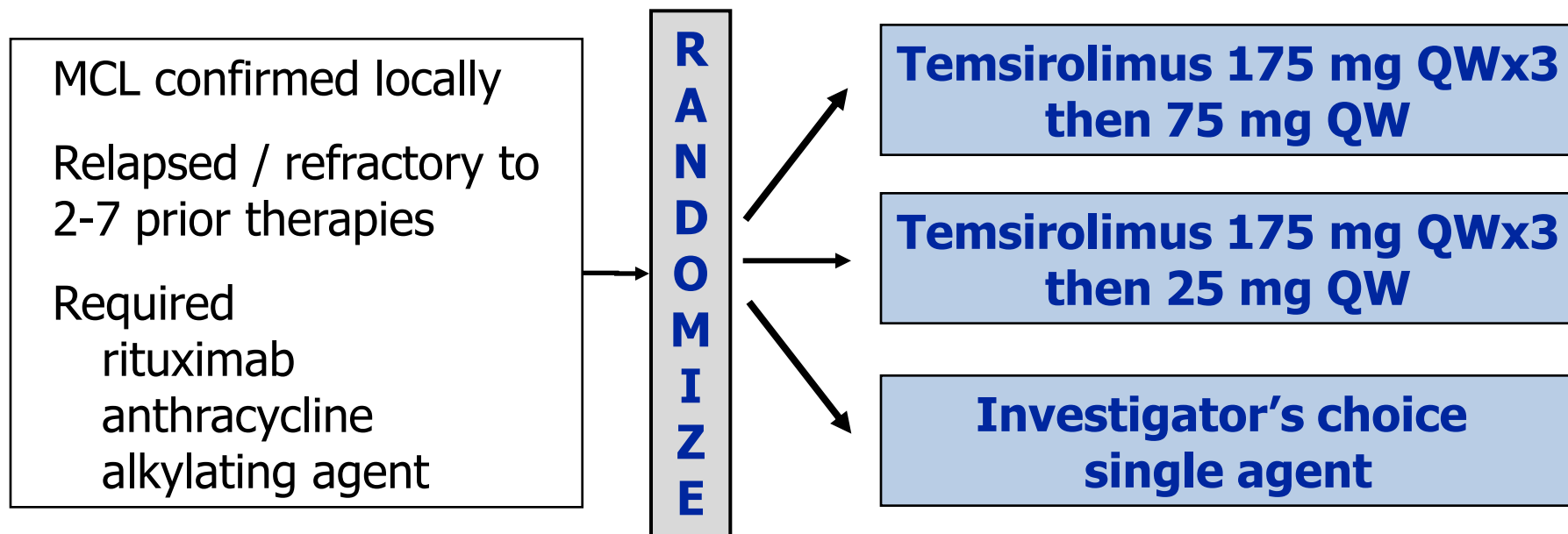
median TTP 6.2 months (median follow-up 13.4 months)

# Kaplan-Meier Estimate for PFS for Lenalidomide in MCL (n = 39)

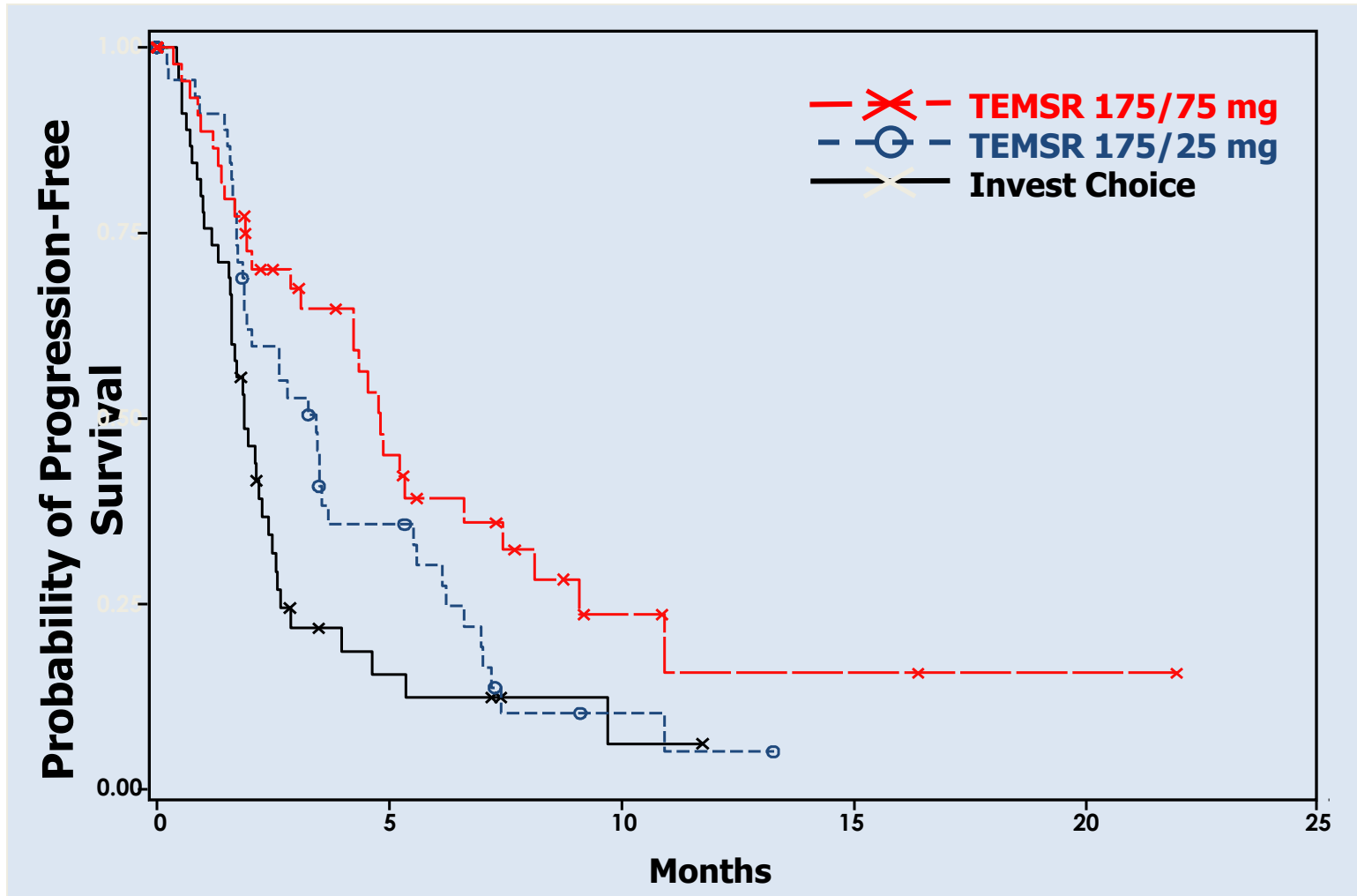


No of subjects	Event	Censored	Median survival (95% CI)
39	49% (19)	51% (20)	216 (75.0–344.0)

# Temsirolimus in MCL



# Progression Free Survival (ITT)



# Conclusions

- Refractory lymphoma
- Some progress during the last years
- Few, if any, durable CR
- No standard
- A lot of new drugs, most of them only tested in phase II studies
- A need for large cooperative studies like in the European MCL Network