GOTEL
Grupo Oncológico para el Tratamiento y Estudio de los Linfomas

XIV CONGRESO NACIONAL DE ONCOLOGÍA MÉDICA

Consolidation treatment with Y^{90} ibritumomab tiuxetan after a new induction regimen in high risk patients according to Follicular International Prognostic Index : A multicentric, prospective Phase II trial of Spanish Lymphoma Oncology Group (GOTEL)

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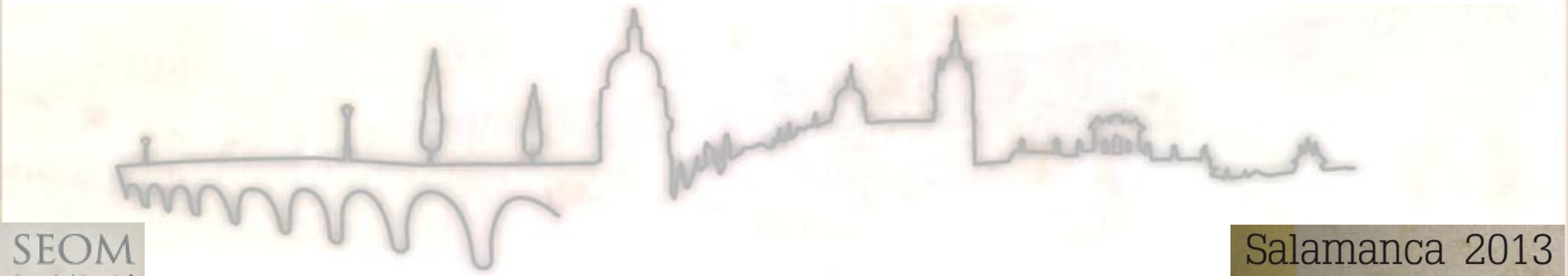
On behalf of the GOTEL (Spanish Lymphoma Oncology Group)



Relapse is the main cause of therapeutic failure in Follicular Lymphoma (FL) . We set out to evaluate the role of consolidation with Y^{90}-Ibritumomab Tiutexan (RIT) in high risk FL patients.

We designed a study with RIT after four cycles of CHOP-R and two CHOP, but without Rituximab.

This study was registered with Clinical Trials.gov, number NCT 00722930, and European number Eudra-CT 2007-00391-19 and was conducted within the GOTEL, a cooperative group set up by a network of Medical Oncology Services in Spain.(www.grupolinfomas.es)

Patients and methods
Patient eligibility

- Patients older than the age of 18 years with biopy-proven, untreated, stage II, III or stage IV follicular non-Hodgkin Lymphoma, grade I, II, or III, expressing the CD 20, PS of 0 to 1.
- All patients required pre-treatment granulocyte cell count of 1500/l or greater and platetet count of 100000/l or greater.
- Patients were excluded if there were HIV positive, if they had central nervous system involvement, if they had received prior chemotherapy, radiotherapy or immunotherapy, had coexistent serious cardiac or a prior malignancy.
- Patients were treated with standard **CHOP-R every 21 days for 4 cycles.**
  - Dosages of 750 mg/m^2 cyclophosphamide, 50 mg/m^2 doxorubicin, and 1,4 mg/m^2 (maximum, 2.0 mg) vincristine, and 100 mg prednisone was given orally daily for 5 days each cycle.

Restaging and inclusion

- Patients were restaged 4 to 8 weeks after completion of the fourth cycle. Patients achieving **at leats an unconfirmed partial response** were elegible for being treated with two cycles with CHOP**, without Rituximab** and **RIT.**

- **Dose Y^{90}-Ibritumomab**: 0.4 mCi/Kg if granulocyte was greater than 1500/L and platelet > 100000/L, and < 25% bone marrow involvent or 0.3 mCi/Kg if platetet were more than 100000 but less than 150000/l, (max. 32 mCi)

- We included 30 patiets from April 2008 and April 2010.
- The survival curves using the Kaplan-Meier method and logrank test.
- An independent data monitoring committee reviewed safety and efficacy data.

Patients and methods

Results

Patients charactistics

Characteristic	Nº	%
Gender		
Male	17	56.7
Female	13	43.3
Histologic grade		
1	9	31.0
2	13	43.3
3	8	24.2
FLIPI risk		
Intermediate	15	50
High	14	46
FLIPI factors		
> 60 y	10	33.3
LDH >	9	30.0
Hb < 12 gr/dl	9	30.0
Stage III/IV	27	90.0
> 4 regions	21	70.0

Clinical Outcomes

•The complete response rate was 76.6 %.

•Of the 18 patients who presented with partial remission to the induction treatment, 11 (61.1%) had Complete Response after the consolidation treatment.

•There was only one exitus due to H1N1 viral pneumonia.

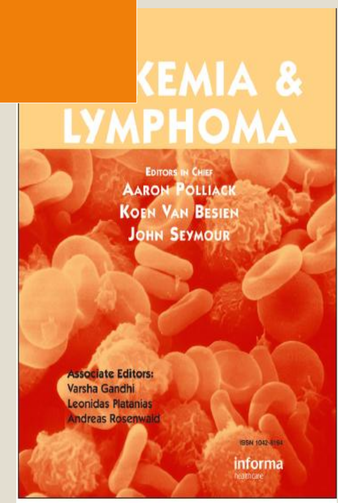
•The most important G3 /4 toxicity was hematological, with 46% thrombopenia and 56% neutropenia.

•None of the patients in the trial died because of FL.

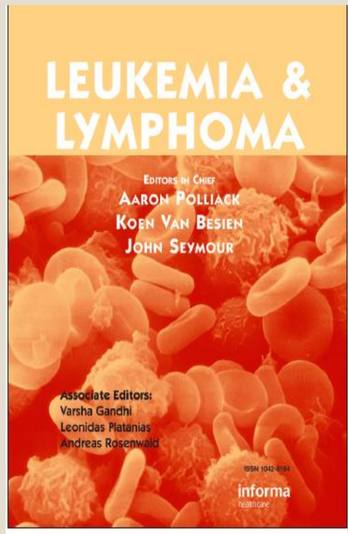
•With median follow-up of 26 months (13-40), the means for disease-free survival or overall survival were not reached.

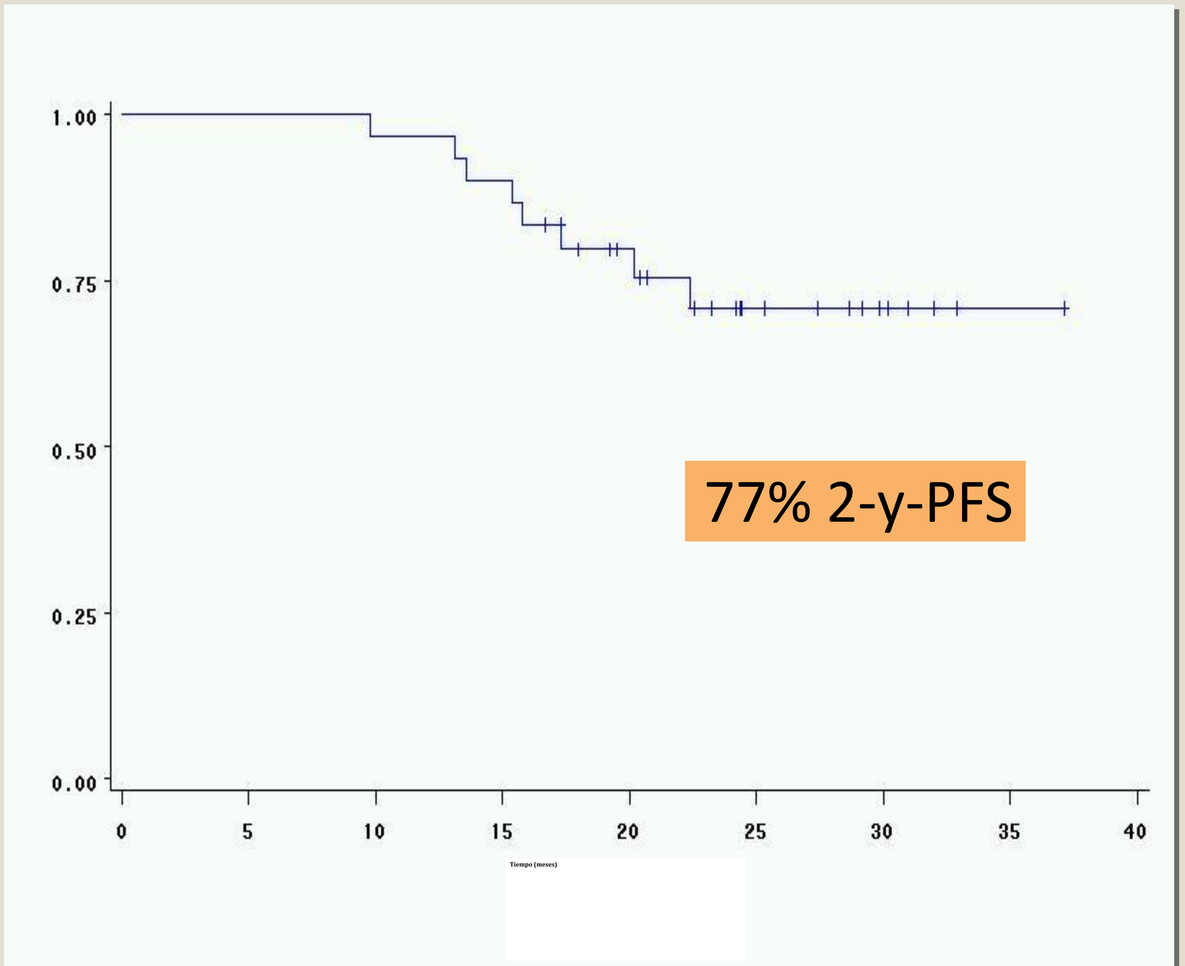
Hematological toxicity per patient

	Grade 1	Grade 2	Grade 1-2	Grade 3	Grade 4	Grade 3-4
Anemia	46.7%	6.7%	53.3%	-	3.3%	3.3%
Leukopenia	30%	16.7%	46.7%	20%	6.7%	26.7%
Neutropenia	10%	6.7%	16.7%	33.3%	23.3%	56.7%
Thrombopenia	13.3%	33.3%	46.7%	33.·3%	23.3%	56.7%

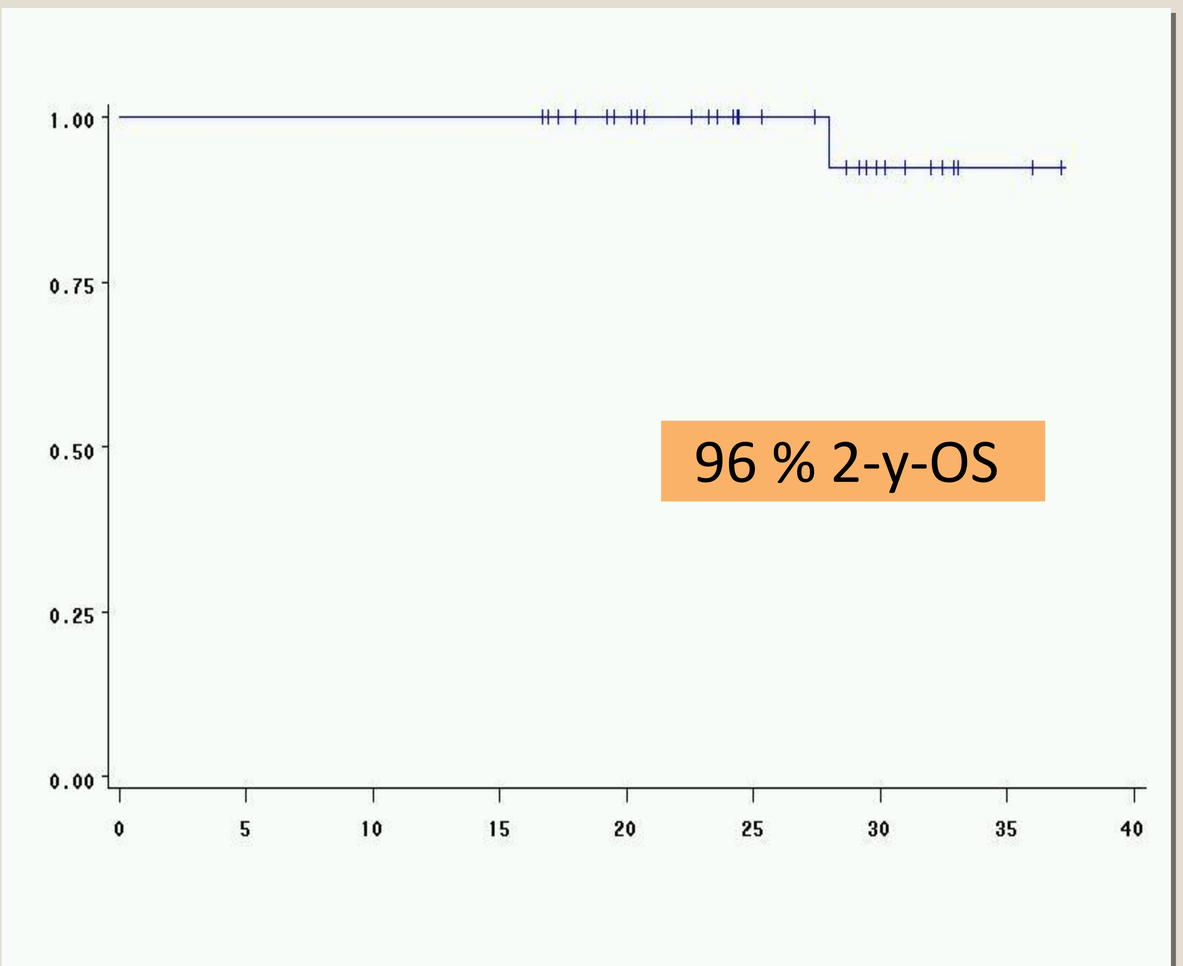


	After 4 CHOP-R		After 2 CHOP		After Consolidation RIT	
	Nº	%	Nº	%	Nº	%
Complete Response	7	23.3	12	40	23	76.6
Partial Response	23	76.6	18	60	5	16.7
Stable Disease	-		-		2	6.7
Total Response	30	100	30	100	30	100





Progression Free Survival



Overall Survival

Conclusions

- The optimal treatment of advanced/high risk FL remains to be determined.

- With the addition of immunotherapy and radioimmunotherapy, the overall and complete response rates have improved

- In our study, with median follow-up of 26 months, we have good results but much longer follow-up will be necessary to determine the durability of these responses