

Prognostic impact of cell of origin profile in young patients with high risk diffuse large B cell lymphoma: results of the BIO-DLCL04 trial of Fondazione Italiana Linfomi

Chiappella A, Agostinelli C, Martelli M, Righi S, Evangelista A, Novero D, Gotti M, Carella AM, Stelitano C, Rossi G, Angelucci E, Balzarotti M, Gaidano G, Ladetto M, Pileri SA and Vitolo U.
On behalf of Fondazione Italiana Linfomi,

INTRODUCTION AND AIM

- The prognostic role of COO assessed by IHC is controversial in Rituximab era.
- FIL conducted a phase III randomized trial aimed at investigating the benefit of intensification with high dose therapy + autotransplant (R-HDC+ASCT) compared to R-dose-dense therapy as first line in young DLBCL at poor risk (aa-IPI 2-3). (Vitolo, ASH 2012).
- The aim of BIO-DLCL04 was to correlate the biological markers with PFS.**

PATIENTS AND METHODS

- From 2005 to 2010, 412 untreated DLBCL at aa-IPI 2-3 were enrolled.
- Central histology revision was mandatory; 13 patients were excluded due to different histologies.
- Biological markers were analyzed on DLBCL NAS
- COO analysis was performed by IHC and cases were classified in germinal center (GC) and non-GC according to Hans' algorithm; COO assessed by Nanostring is ongoing.
- BCL2, BCL6 and MYC anomalies were tested by IHC and by FISH (ongoing).
- Cases were deemed positive if at least 30% of lymphoma cells were stained with each antibody (with the exception of at least 40% for MYC).

RESULTS

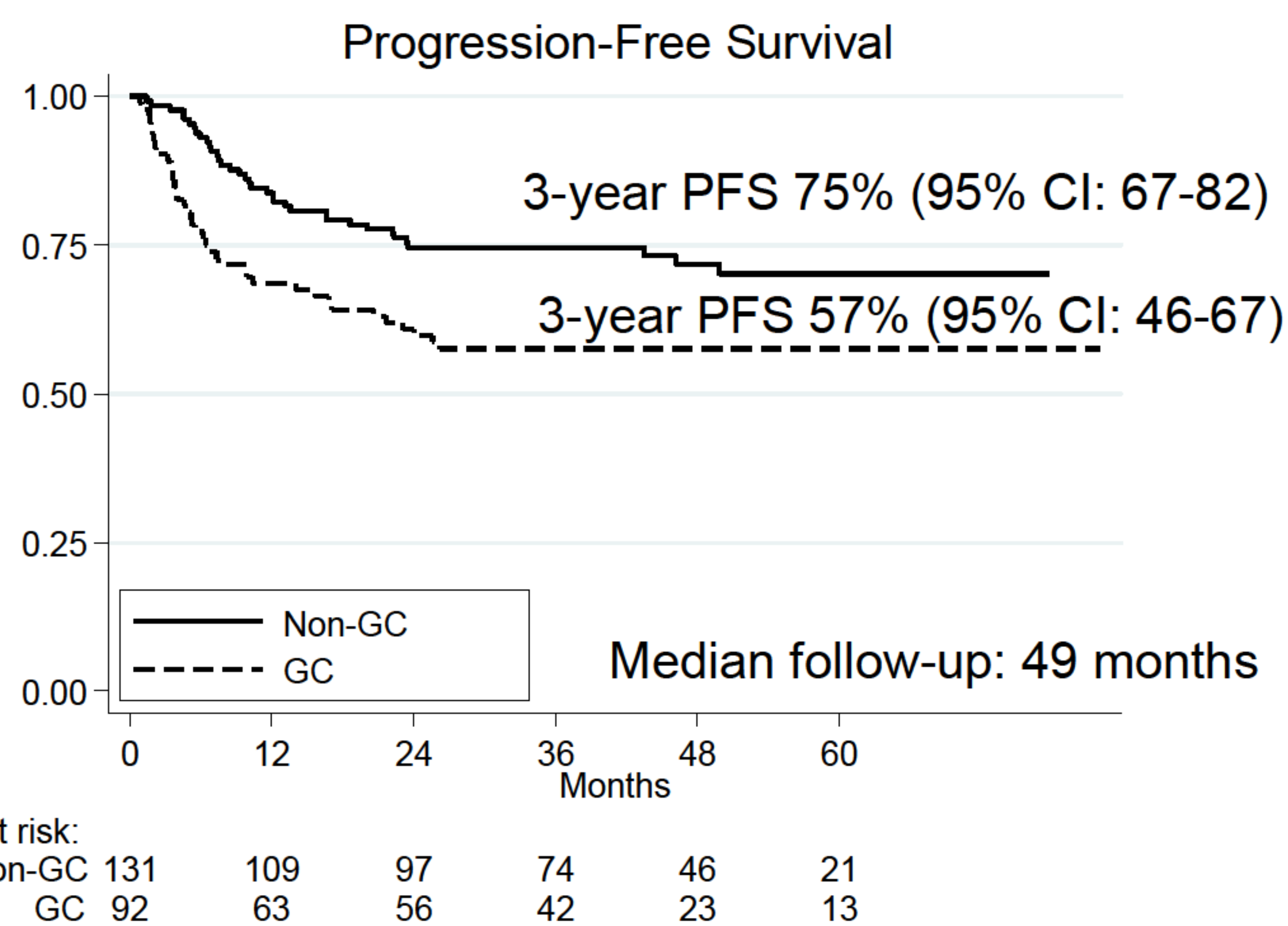
223 DLBCL NAS were analyzed: 131 non-GC and 92 GC; BCL2, BCL6 and MYC anomalies were tested in 196, 74 and 107 cases.

CLINICAL CHARACTERISTICS

	Non-GC (N=131)	GC (N=92)
Median age	51 years	51 years
Male	49%	45%
aa-IPI 3	15%	25%
BM-involvement	16%	24%
R-HDC+ASCT	45%	49%

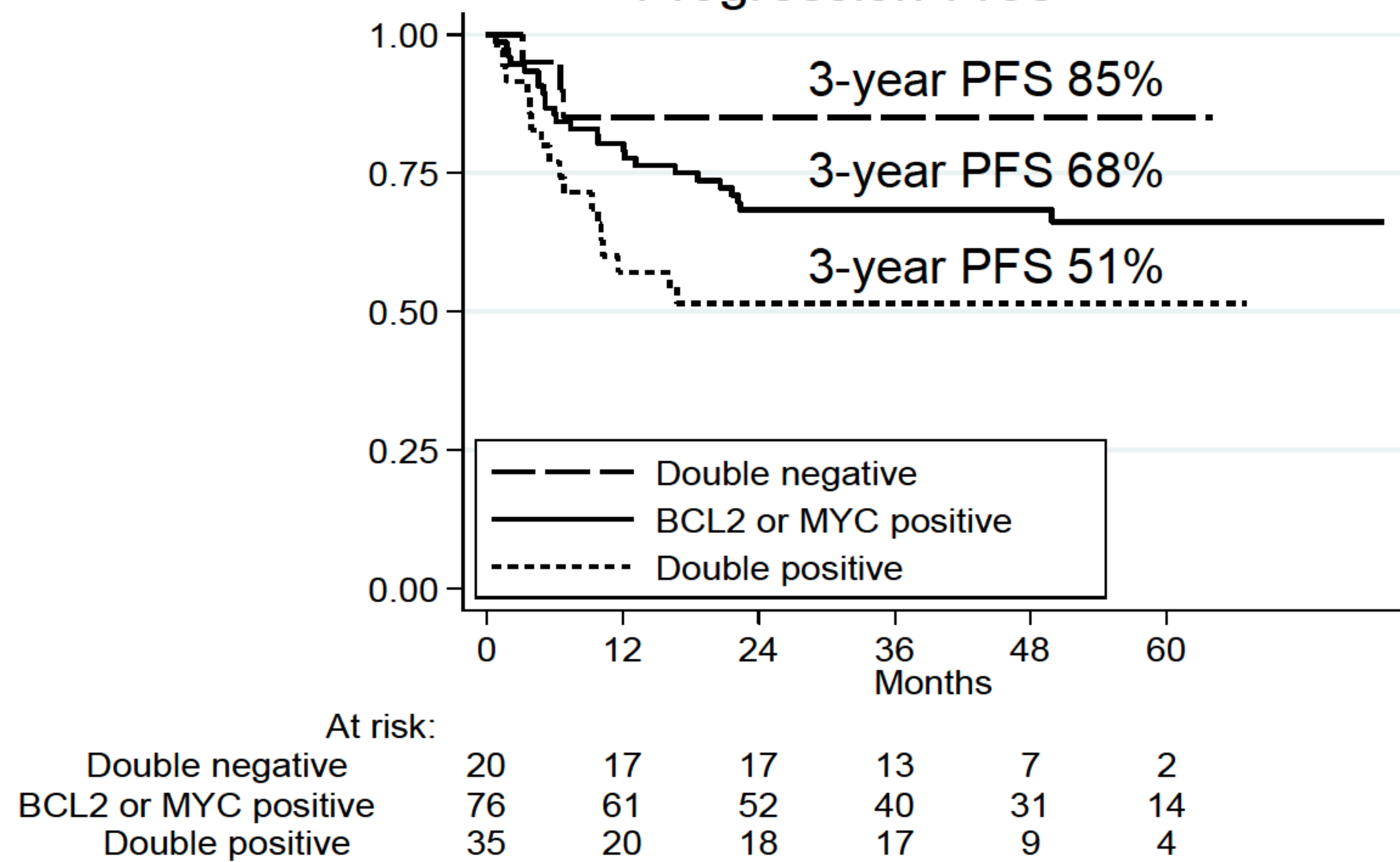
COMPLETE RESPONSE, PET NEGATIVE

Non-GC	GC
105 (80%)	62 (67%)



HR 0.55 (0.35-0.87), p.01
aHR (for age, gender, aa-IPI, BM) 0.56 (0.35-0.88), p.013

Progression-Free



Overexpression of MYC by IHC: aHR 1.84 (0.99-3.44), p.054.
aHR for double expressers compared to double negative of 3.91 (1.13-13.53),

CONCLUSIONS

- In conclusion, with the limit of the analysis performed by IHC based on Hans' algorithm, BIO-DLCL04 showed an unexpected better outcome for non-GC compared to GC, irrespective of treatment arm.
- The ongoing analysis conducted by Nanostring will be more informative.
- The overexpression of MYC, single or associate to BCL2 overexpression, was confirmed as relevant prognostic role.
- The final analysis by FISH is ongoing.

