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## Objectives

1. Assess overall survival (OS) in follicular lymphoma (FL) benchmarked to the general population
2. Assess outcome of FL patients at diagnosis as well as stratified by event status 12 months from diagnosis (EFS12)

## Methods

- Patients with newly diagnosed grade 1-3a FL were prospectively enrolled in University of Iowa/Mayo Clinic Lymphoma SPORE Molecular Epidemiology Resource (MER) from 2002-2012
- Patient management and therapy (including observation i.e. watchful waiting) was standard of care per treating physician
- Event free survival (EFS) was defined as time from diagnosis to relapse/progression, re-treatment, or death due to any cause
- EFS12 defined as EFS status 12 months after diagnosis
- OS for MER FL patients compared to age and sex matched US population via standardized mortality ratios (SMR)
- Replication performed in a dataset of 412 patients diagnosed with FL between 2002-2010 from Lyon, France hospital registries (N=150 from Centre Léon Bérard, N=262 from Lyon-Sud)
- Lyon patients compared to French population

## Patient Characteristics (MER)

- 920 patients with newly diagnosed FL
- Median age at diagnosis: 60 years (range 19-93); 52% male
- Median follow-up of 71 months (range 5-144)
- 453 events (49%) and 130 deaths (14%)
- 83% achieved EFS12, 71% achieved EFS24
- 87% grade 1-2, 13% grade 3a;
- 40% FLIPI 0-1, 34% FLIPI 2, 26% FLIPI 3-5
- Management at diagnosis: 35% OBS, 12% R monotherapy, 38% immunochemotherapy (IC), 15% other

## Results

- Overall survival from FL diagnosis in the MER was slightly inferior to the age and sex matched general population in the US: SMR=1.14, 95% CI: (0.96-1.36)
- First events occurring in the first 12 months from diagnosis (Fail EFS12) were strongly associated with poor subsequent OS (SMR=3.72, 95% CI: 2.84-4.89)
- Patients achieving EFS12 had excellent subsequent OS: (SMR=0.73, 95% CI: 0.57-0.94)
- Results replicated in French dataset compared to French population
- First events occurring between 12 and 24 months from diagnosis were associated with inferior OS (SMR=1.62, 95% CI: 1.06-2.48) but with a weaker effect than failing EFS12
- First events occurring beyond 24 months were not significantly associated with inferior subsequent OS (SMR=0.98, 95% CI: 0.54-1.76)

## Table 1

Cohort	Patient subgroup	N	% Fail EFS12	SMR (95% CI) From Diagnosis	SMR (95% CI) From Fail EFS12	SMR (95% CI) From Achieve EFS12
MER	All FL patients	920	17%	1.14 (0.96-1.36)	3.72 (2.84-4.89)	0.73 (0.57-0.94)
MER	Grade 1-2	801	18%	1.13 (0.94-1.37)	3.46 (2.59-4.64)	0.75 (0.57-0.97)
MER	Grade 3a	119	13%	1.21 (0.77-1.89)	7.13 (3.40-15.0)	0.64 (0.32-1.27)
MER	≤60	480	17%	2.08 (1.51-2.85)	9.58 (6.47-14.2)	0.89 (0.51-1.57)
MER	>60	440	18%	0.97 (0.79-1.18)	2.38 (1.63-3.47)	0.70 (0.53-0.93)
MER	Observed at dx	326	19%	0.83 (0.60-1.14)	1.44 (0.80-2.60)	0.70 (0.47-1.05)
MER	R alone at dx	111	15%	0.64 (0.34-1.19)	3.73 (1.20-11.6)	0.46 (0.21-1.03)
MER	IC at dx	349	14%	1.83 (1.41-2.37)	17.63 (12.4-25.1)	0.73 (0.46-1.16)
MER	FLIPI 0-1	366	13%	0.77 (0.54-1.11)	2.61 (1.36-5.02)	0.64 (0.41-1.01)
MER	FLIPI 2	312	20%	1.20 (0.91-1.59)	3.52 (2.34-5.30)	0.72 (0.47-1.11)
MER	FLIPI 3-5	242	21%	1.48 (1.13-1.95)	5.00 (3.23-7.76)	0.85 (0.56-1.29)
Lyon	All FL patients	412	18%	1.76 (1.29-2.41)	8.74 (5.70-13.4)	1.02 (0.62-1.66)
Lyon	≤60	240	18%	3.37 (2.17-5.22)	12.30 (7.00-21.7)	1.71 (0.82-3.59)
Lyon	>60	172	18%	1.17 (0.75-1.84)	6.30 (3.28-12.1)	0.77 (0.40-1.49)
Lyon	IC at dx	251	14%	2.17 (1.47-3.18)	20.88 (12.4-35.3)	1.09 (0.59-2.03)

Fig. 1: MER OS from diagnosis

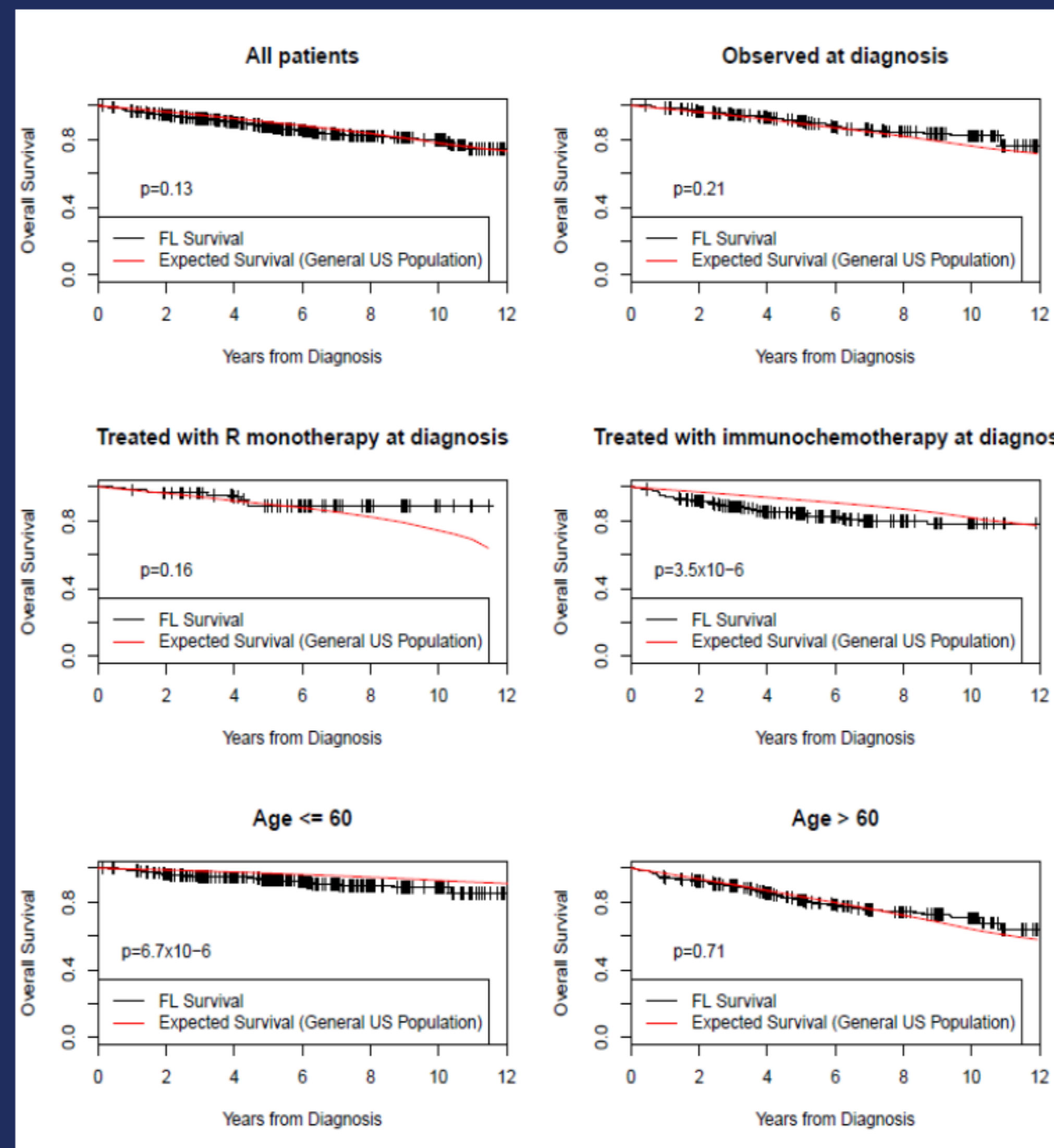
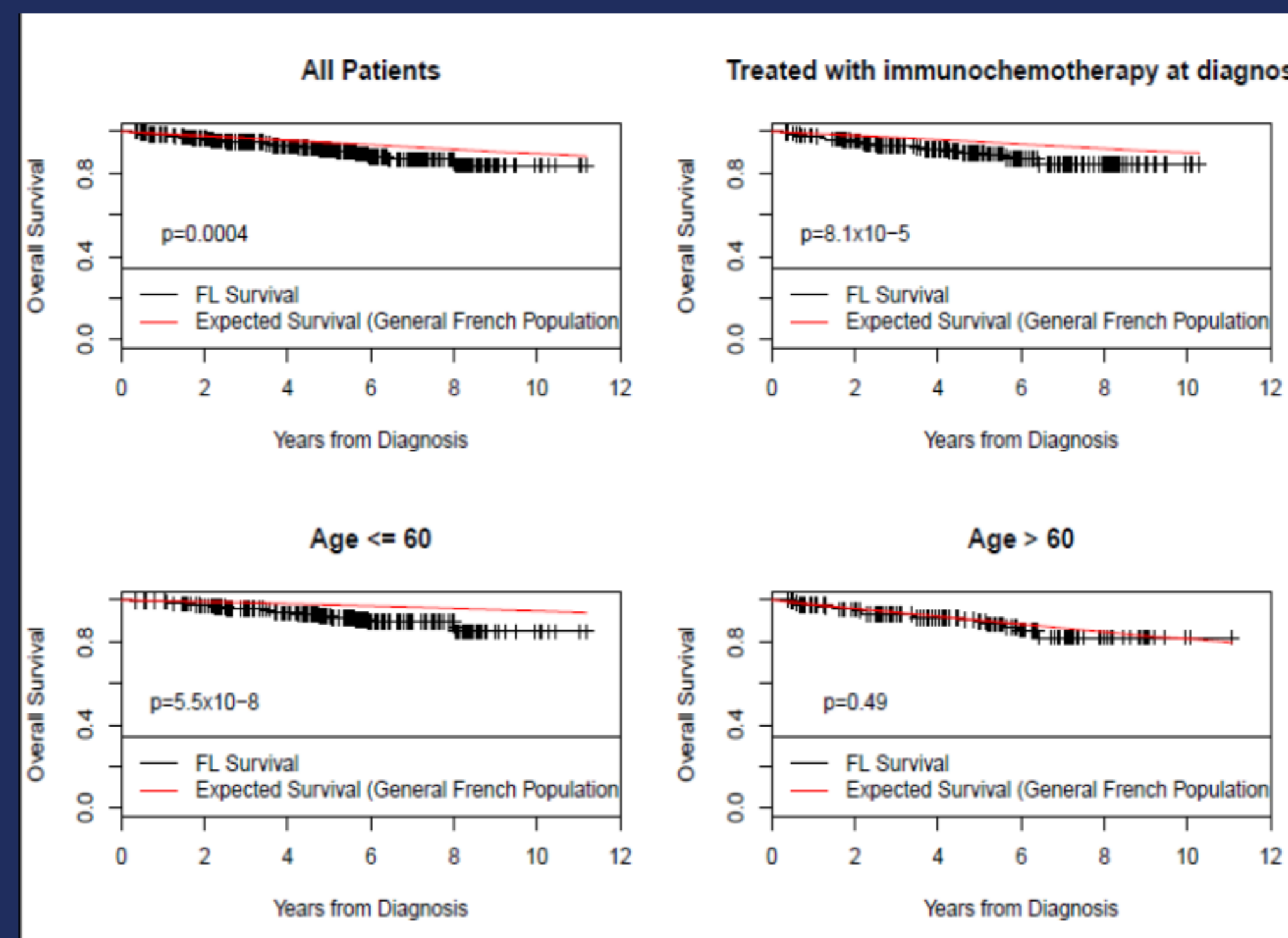
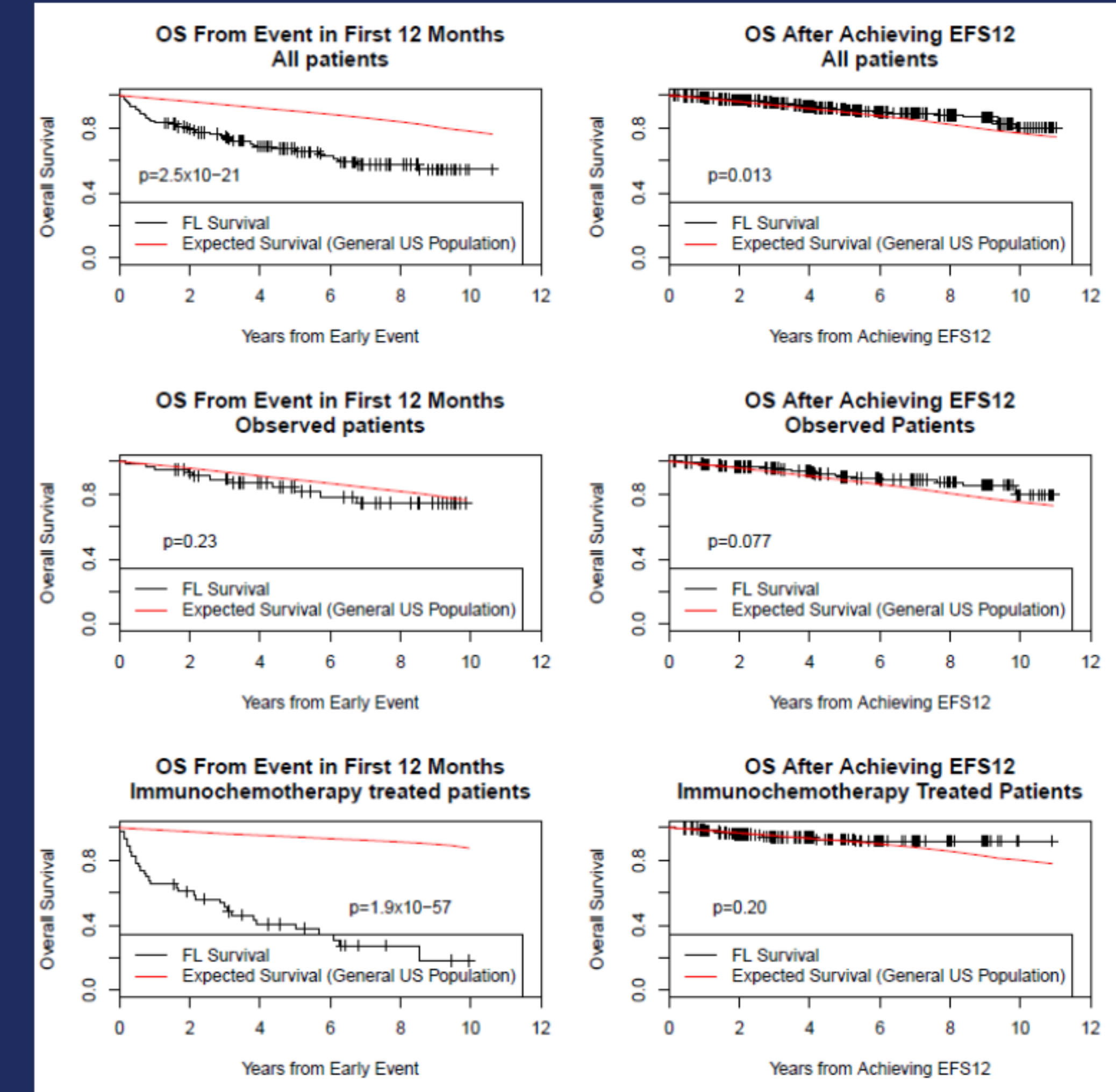


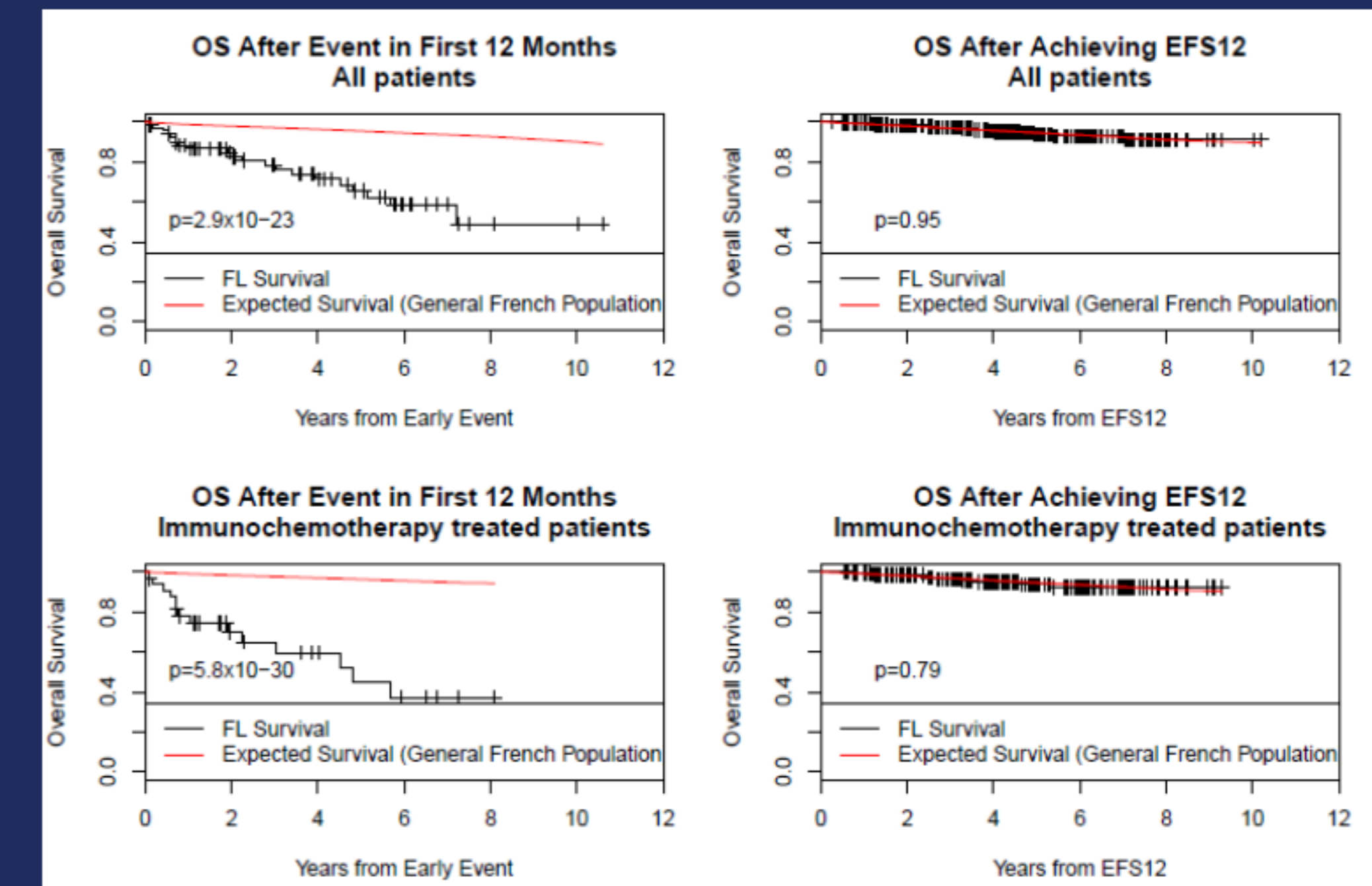
Fig. 2: Lyon OS from diagnosis



## Fig. 3: MER OS from EFS12 event



## Fig. 4: Lyon OS from EFS12 event



## Conclusions

- Survival from FL at diagnosis is similar to the general population
- Patients selected at diagnosis for non-intensive therapy (perhaps reflecting low-burden disease) have excellent outcome without survival deficit for the first 10 years from diagnosis
- Patients requiring initial treatment with immunochemotherapy have a survival deficit from diagnosis compared to population
- Reassessment of status at 12 months from diagnosis stratifies patients on future outcome independent of baseline prognostic features such as age or FLIPI
- Progression or re-treatment in the first year after FL diagnosis is associated with significant survival deficit
- No progression or re-treatment in the first year after FL diagnosis is associated with excellent subsequent survival, even in high-risk patient subsets.
- Patients with early events should be focus of future studies and novel agents in follicular lymphoma
- The greatest is among patients with an early event after initial immunochemotherapy

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