Multicohort Study of Conditional Survival and Cause of Death After Achieving Event-Free Survival at 24 Months (EFS24) in Patients With Mantle Cell Lymphoma

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BACKGROUND

- Mantle cell lymphoma (MCL) is generally considered incurable, but survival outcomes are improving in the evolving treatment landscape.
- Event-free survival status at a landmark (e.g., 24 months) after frontline immunochemotherapy may help identify patients with lymphoma who will subsequently do well, which would be useful for patient counseling, care planning, and trial design.
- Event-free survival at 24 months (EFS24) is an established important endpoint in diffuse large B-cell lymphoma and follicular lymphoma, but the role of EFS24 in MCL has not been well defined.
- To investigate the role of EFS24 in MCL, we evaluated conditional survival and cause of death in patients with MCL who achieved EFS24 after frontline immunochemotherapy.

METHODS

- Outcomes after frontline immunochemotherapy were evaluated in 3 cohorts: Mayo/Iowa MER prospective clinic-based cohort, BC Cancer retrospective population-based cohort, and Swedish Lymphoma Registry.
- For each cohort, two treatment eras were defined based on the specifics of local treatment patterns.
- Overall survival (OS) after diagnosis and after achieving EFS24 was compared to the background age- and sex-matched general population using a standardized mortality ratio (SMR).
- Cumulative incidence of lymphoma-specific death was analyzed using Gray's test, with deaths from all other causes treated as competing events.

CONCLUSIONS

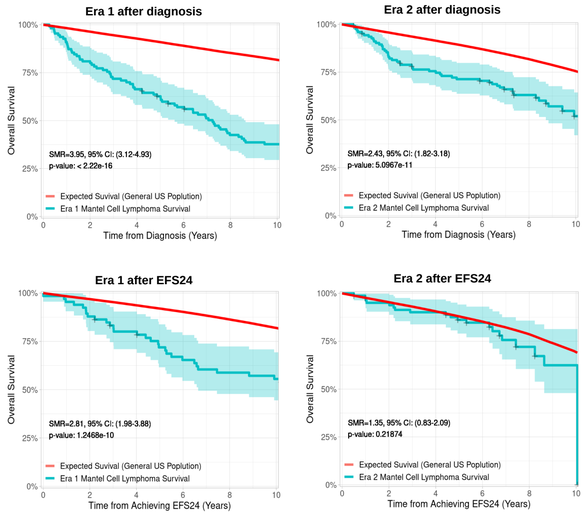
- In all three cohorts, overall survival of patients who achieve EFS24 after frontline immunochemotherapy improved in the more recent treatment era and moved closer to the expected background survival of the general population.
- Of particular note, in all 3 cohorts, after achieving EFS24, lymphoma-related mortality was no longer the leading cause of death in the more recent treatment era.
- EFS24 following frontline treatment may become a critical landmark for predicting subsequent outcomes in patients with MCL in the modern era.

RESULTS

Table 1. Comparison of Treatment Patterns in Era 1 vs Era 2

Cohort	Era 1	Era 2
Mayo/Iowa MER	Era M1 (2002 – 2009) n=110	Era M2 (2010 – 2015) n=127
	• More R-HyperCVAD (15%) • Minimal Nordic or R-CHOP/R-DHAP (1%) • More R-CHOP (84%) • No BR (0%)	• Fewer R-HyperCVAD (6%) • More Nordic or R-CHOP/R-DHAP (21%) • Fewer R-CHOP (34%) • More BR (39%)
BC Cancer	Era B1 (2003 – 5/2013) n=250	Era B2 (6/2013 – 2019) n=188
	• Nearly universal R-CHOP (99%) • Minimal BR (1%)	• Minimal R-CHOP (1%) • Nearly universal BR (99%)
Swedish	Era S1 (2006 – 2012) n=442	Era S2 (2013 – 2018) n=439
	• Similar Nordic (37%) • More R-CHOP (24%) • Fewer BR (18%) • More other IC (21%)	• Similar Nordic (33%) • Fewer R-CHOP (11%) • More BR (51%) • Minimal other IC (5%)

Fig 1. OS in the MER Cohort Benchmarked to General US Population



RESULTS (Cont')

Fig 2. OS in the BC Cancer Cohort Benchmarked to General British Columbia Population

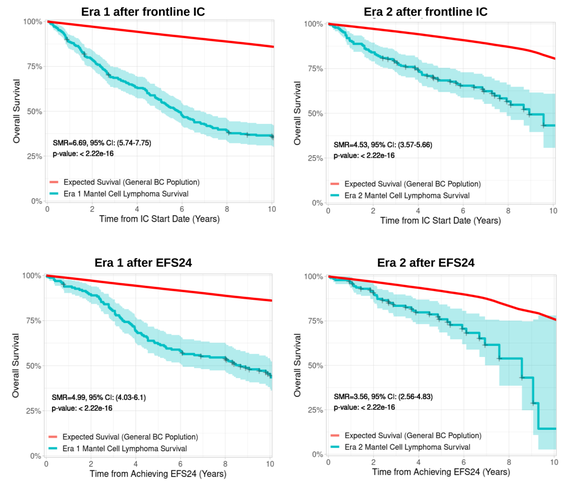


Fig 3. OS in the Swedish Cohort Benchmarked to General Swedish Population

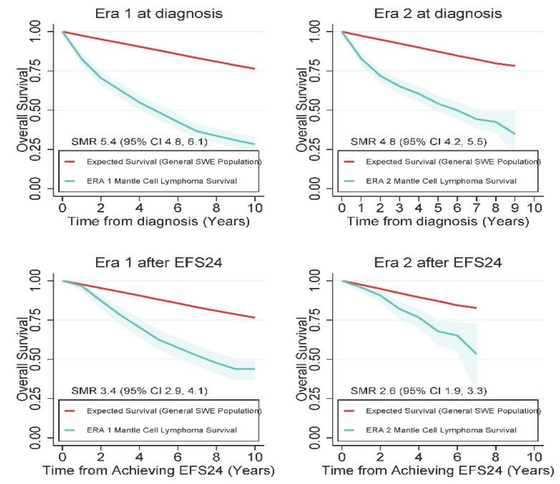


Table 2. Cumulative Incidences of Lymphoma Related vs Lymphoma Unelated Deaths Stratified by Cohort, Era, and Landmark

Cohort	Era	Cause of death	Cause-specific mortality rate			
			2 years from diagnosis	5 years from diagnosis	2 years from achieving EFS24	5 years from achieving EFS24
Mayo/Iowa MER	Era M1 (2002 – 2009)	Lymphoma	14% (9% – 22%)	26% (19% – 35%)	6% (2% – 16%)	21% (13% – 33%)
		Non-Lymphoma	1% (0% – 7%)	6% (3% – 12%)	6% (2% – 16%)	8% (3% – 18%)
		Unknown	5% (2% – 11%)	6% (3% – 13%)	0%	0%
	Era M2 (2010 – 2015)	Lymphoma	15% (10% – 23%)	20% (14% – 28%)	**0%**	**1% (0% – 9%)**
		Non-Lymphoma	2% (0% – 7%)	6% (3% – 12%)	**5% (3% – 13%)**	**5% (2% – 13%)**
		Unknown	0%	3% (1% – 9%)	**0%**	**8% (4% – 17%)**
BC Cancer	Era B1 (2003 – 5/2013)	Lymphoma	19% (15% – 24%)	40% (34% – 47%)	9% (6% – 15%)	33% (26% – 41%)
		Non-Lymphoma	2% (1% – 5%)	4% (2% – 7%)	1% (0% – 5%)	6% (3% – 10%)
	Era B2 (6/2013 – 2019)	Lymphoma	14% (10% – 20%)	23% (17% – 30%)	**6% (3% – 11%)**	**12% (7% – 19%)**
		Non-Lymphoma	2% (1% – 6%)	9% (6% – 14%)	**4% (2% – 13%)**	**13% (8% – 20%)**
Swedish	Era S1 (2006 – 2012)	Lymphoma	23% (20% – 27%)	41% (36% – 46%)	8% (5% – 12%)	23% (18% – 29%)
		Non-Lymphoma	6% (4% – 9%)	10% (7% – 13%)	5% (2% – 8%)	14% (10% – 19%)
	Era S2 (2013 – 2018)	Lymphoma	24% (20% – 28%)	33% (29% – 38%)	**4% (2% – 7%)**	**13% (9% – 19%)**
		Non-Lymphoma	5% (3% – 7%)	12% (9% – 16%)	**5% (3% – 9%)**	**19% (13% – 26%)**

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