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POSTER ABSTRACTS

623.MANTLE CELL, FOLLICULAR, AND OTHER INDOLENT B CELL LYMPHOMAS: CLINICAL AND EPIDEMIOLOGICAL

An International Multicohort Study of Conditional Survival and Cause of Death after Achieving Event-Free Survival at 24 Months in Patients with Mantle Cell Lymphoma

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Background: Event-free survival at 24 months (EFS24) after frontline immunochemotherapy (IC) is an important endpoint in diffuse large B-cell lymphoma and follicular lymphoma, and patients who achieve EFS24 have similar survival compared to age- and sex-matched general population. The role of EFS24 in predicting subsequent survival has not been established in mantle cell lymphoma (MCL), possibly due to perceived poor survival historically. In the last decade, the outcomes of MCL are improving in the evolving treatment landscape. In this international multicenter study, we investigated conditional survival and cause of death in patients with MCL who achieved EFS24 after frontline IC in the older and more recent eras.
Methods: Outcomes after frontline IC were evaluated in 5 independent cohorts that included over 3000 patients in total: Mayo/Iowa MER prospective cohort, BC Cancer retrospective population-based cohort, US 12-center retrospective cohort, Swedish Lymphoma Registry, and Danish National Lymphoma Registry. For each cohort, 2 treatment eras were defined based on cohort-specific shifts in treatment patterns (Table 1). Overall survival (OS) after diagnosis and after achieving EFS24 were compared to the background age- and sex-matched general population using a standardized mortality ratio (SMR). Cumulative incidences of cause-specific deaths were analyzed using a competing risk model.
Results: In the MER cohort, patients treated in Era M1 (2002-2009; n=147) and Era M2 (2010-2015; n=153) both had inferior OS compared to the general US population. A lower SMR in Era M2 vs M1 (2.25 vs 3.46) suggests a narrower gap in OS compared to the general US population. Lymphoma was the leading cause of death in both eras. In Era M1, patients who achieved EFS24 still had inferior OS compared to the general US population (SMR=2.40, 95% CI 1.76-3.19), and lymphoma remained the leading cause of death. For patients in Era M2 who achieved EFS24, the difference in OS compared to the general US population was not statistically significant with current follow-up (SMR=1.43, 95% CI 0.93-2.09), and lymphoma was no longer the leading cause of death (Table 2).
In the BC cohort, patients treated in Era B2 (6/2013-2019; n=188) vs Era B1 (2003-5/2013; n=250) had a narrower gap in OS compared to the general British Columbia population (SMR 4.53 vs 6.69). Lymphoma was the leading cause of death in both eras. For patients achieving EFS24, the gap in OS was narrower in Era B2 vs B1 (SMR 3.56 vs 4.99). After achieving EFS24, lymphoma was the single leading cause of death for patients in Era B1 but not in Era B2 (Table 2).
In the US 12-center cohort, patients treated in Era U1 (2002-2011; n=312) and Era U2 (2012-2016; n=417) both had inferior OS compared to the general US population (SMR 2.68 and 2.92, respectively). In patients who achieved EFS24, with current follow up, the difference in OS compared to the general US population was statistically significant in Era U1 (SMR=2.01, 95% CI 1.50-2.64) but not in Era U2 (SMR=1.44, 95% CI 0.82-2.34). Lymphoma was not the leading cause of death after achieving EFS24 (Table 2).
In the Swedish cohort, the gap in OS compared to the general Swedish population was narrower in Era S2 (2013-2018; n=439) vs S1 (2006-2012; n=442), both after frontline IC (SMR 4.8 vs 5.4) and after achieving EFS24 (SMR 2.6 vs 3.4). After achieving EFS24, lymphoma was the leading cause of death for patients in Era S1 but not in Era S2 (Table 2).
In the Danish cohort, patients treated in Era D2 (2014-2020; n=370) vs Era D1 (2004-2013; n=461) had a slightly narrower gap in OS compared to the general Danish population (SMR 1.90 vs 2.10). For patients who achieved EFS24, those in Era D1 still had inferior OS compared to the general Danish population (SMR=1.44, 95% CI 1.22-1.68), but the OS difference compared to the general Danish population in Era D2 was not statistically significant (SMR=1.27, 95% CI 0.92-1.72) with current follow-up (Table 2). Cause of death data were not available in this cohort.
Conclusion: Survival in patients with MCL who achieved EFS24 after frontline IC improved in the more recent treatment era and moved closer to the background expected survival. After achieving EFS24, lymphoma-related mortality was no longer the leading cause of death in the more recent era. EFS24 following frontline treatment may become a critical endpoint for predicting subsequent outcomes in patients with MCL in the modern era.

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

Cohort	Era 1	Era 2
Mayo/Iowa MER	Era M1 (2002–2009), n=147	Era M2 (2010–2015), n=153
	• More R-HyperCVAD (12%) • Minimal Nordic or R-CHOP/R-DHAP (1%) • More R-CHOP/R-CHOP-like (65%) • Minimal BR (1%) • More other immunochemotherapy (22%)	• Fewer R-HyperCVAD (8%) • More Nordic or R-CHOP/R-DHAP (22%) • Fewer R-CHOP/R-CHOP-like (24%) • More BR (41%) • Minimal other immunochemotherapy (6%)
BC Cancer	Era B1 (2003–5/2013), n=250	Era B2 (6/2013–2019), n=188
	• Near universal R-CHOP (99%) • Minimal BR (1%)	• Minimal R-CHOP (1%) • Near universal BR (99%)
US 12-Center	Era U1 (2002–2010), n=312	Era U1 (2011–2016), n=417
	• Similar high dose AraC-based (39%) • More R-CHOP/R-CHOP-like (53%) • Fewer BR-based (8%)	• Similar high dose AraC-based (37%) • Fewer R-CHOP/R-CHOP-like (20%) • More BR-based (43%)
Sweden	Era S1 (2006–2012), n=442	Era S2 (2013–2018), n=439
	• Similar Nordic (37%) • More R-CHOP/R-CHOP-like (24%) • Fewer BR (18%) • More other immunochemotherapy (21%)	• Similar Nordic (33%) • Fewer R-CHOP/R-CHOP-like (11%) • More BR (51%) • Minimal other immunochemotherapy (5%)
Denmark	Era D1 (2004–2013), n=461	Era D2 (2014–2020), n=370
	• More Nordic (37%) • More R-CHOP/R-CHOP-like (41%) • Fewer BR (9%) • Similar other immunochemotherapy (13%)	• Fewer Nordic (22%) • Fewer R-CHOP/R-CHOP-like (17%) • More BR (45%) • Similar other immunochemotherapy (16%)

Table 2. Overall Survival Compared to Age- and Sex-Matched General Population and Cause of Death After EFS24

Cohort	Era	SMR after diagnosis	SMR after EFS24	Cause-specific mortality rate				
				Cause of death	2 years from diagnosis	5 years from diagnosis	2 years from EFS24	5 years from EFS24
Mayo/Iowa MER	Era M1 (2002–2009)	3.46 (2.84–4.18) n=147	2.40 (1.76–3.19) n=78	Lymphoma	20% (14%–27%)	33% (26%–41%)	6% (3%–15%)	18% (11%–29%)
				Non-Lymphoma	1% (0%–5%)	5% (3%–11%)	4% (1%–12%)	8% (4%–17%)
				Unknown	3% (1%–8%)	5% (3%–11%)	0%	1% (0%–9%)
	Era M2 (2010–2015)	2.25 (1.73–2.88) n=153	1.43 (0.93–2.09) n=100	Lymphoma	15% (10%–22%)	21% (15%–29%)	3% (1%–9%)	8% (4%–16%)
				Non-Lymphoma	2% (0%–6%)	8% (5%–14%)	7% (4%–15%)	9% (5%–17%)
				Unknown	1% (0%–5%)	2% (1%–6%)	1% (0%–7%)	2% (0%–8%)
BC Cancer Agency	Era B1 (2003–5/2013)	6.69 (5.75–7.75) n=250	4.99 (4.03–6.10) n=164	Lymphoma	19% (15%–24%)	40% (34%–46%)	9% (5%–14%)	31% (25%–39%)
				Non-Lymphoma	2% (1%–5%)	4% (2%–7%)	2% (1%–6%)	7% (4%–12%)
	Era B2 (6/2013–2019)	4.53 (3.57–5.66) n=188	3.56 (2.56–4.83) n=147	Lymphoma	14% (10%–20%)	23% (17%–29%)	6% (3%–12%)	12% (7%–20%)
				Non-Lymphoma	2% (1%–6%)	9% (6%–15%)	3% (1%–7%)	12% (7%–19%)
US 12-Center	Era U1 (2002–2010)	2.68 (2.18–3.27) n=312	2.01 (1.50–2.64) n=233	Lymphoma	4% (2%–7%)	9% (7%–13%)	3% (1%–6%)	8% (5%–12%)
				Non-Lymphoma	6% (4%–9%)	12% (9%–17%)	3% (2%–7%)	9% (6%–14%)
	Era U2 (2011–2016)	2.92 (2.29–3.67) n=417	1.44 (0.82–2.34) n=231	Lymphoma	6% (4%–9%)	13% (9%–18%)	4% (2%–8%)	6% (3%–14%)
				Non-Lymphoma	5% (4%–8%)	12% (9%–17%)	3% (1%–7%)	8% (3%–17%)
Sweden	Era S1 (2006–2012)	5.4 (4.8–6.1) n=442	3.4 (2.9–4.1) n=245	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)	4.8 (4.2–5.5) n=439	2.6 (1.9–3.3) n=271	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%)
Denmark	Era D1 (2004–2013)	2.10 (1.87–2.34) n=461	1.44 (1.22–1.68) n=290	Not Available	–	–	–	–
	Era D2 (2014–2020)	1.90 (1.58–2.25) n=370	1.27 (0.92–1.72) n=237		–	–	–	–

Abbreviations: EFS24, event-free survival at 24 months; SMR, standard mortality ratio (compared to age- and sex-matched general population and reported with 95% confidence interval).

Figure 1

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