HoLISTIC Modeling Meeting

5.25.23

Susan, Angie, Nick, Andy, John

* Eligibility criteria unless otherwise specified: Age 18-65y; cHL; early stage disease; no out of range lab values (albumin 1-6; ESR >=1; hemoglobin 5-16.5; lymphocyte count 0.1-5; WBC count 0.1-50); no above & below diaphragm disease; no Waldeyer’s ring only; no count of 0 nodal groups (looking above & below diaphragm); missing <50% of candidate predictors. Registries further restricted to: treated with curative intent; not treated on a trial; diagnosed 1996 to 2019
* Angie shared Table 1. Nodal Locations by Study Type
	+ Small difference between registry and trials
	+ New version of combining nodal locations (mutually exclusive)
		- Will want to collapse these
	+ John: most common combinations Cerv/Supralav/Occip AND Mediastinum/Hilum + Cerv/Supralav/Occip ONLY matches data
* Angie shared Table 2. Univariate results for nodal locations for 5y PFS for development cohort
	+ Cervical group was protective, others had increased risk
	+ Reference is now cervical
		- Andy: will need to think about collapse (by HR or clinical)
		- Option 1. Categories: Cerv/Supralav/Occip ONLY, Cerv/Supralav/Occip AND Mediastinum/Hilum, Mediastinum/Hilum ONLY, all 3, merge the rest
		- Option 2. Angie will try collapsing all 3 with all else as well
		- Option 3.
			* Media, media + cerv
			* 3 infra, all 3
			* Cerv only (ref)
		- Option 4. (not mutually exclusive)
			* Cervical only (ref)
			* any infra, excluding cerv
			* any mediastinum, excluding cerv
			* interactions
		- option 5. May end up with just cerv vs all else
* Andy: Nervous to use PMH as validation even for ASH, what about 2/3 1/3 split? Might not be worth it if the registries are missing critical pieces
	+ Trials had clinical restrictions/different distributions of certain variables, so use of PMH leaves us with some unevenness
* Angie: Could do development with 4 trials + PMH and validate with other registries as they come in
* John: leave out nodal locations at this time?
* Susan: development cohort in the trials, see if Ranjana and Rich will run the model in their institution
	+ Andy: not sure about their numbers to use for validation
* Decision to keep development/validation as it: trials as development, PMH as validation
* Angie shared Table 3. Distribution of histology
	+ Collapse histology?
	+ Andy: leave as is and say “we looked at it and nothing came out”
* Age relationship with 5y PFS for development cohort

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|  | Summary Statistics |
| Age (years), mean (SD) | 34.6 (12.3) |
| Age (years), median (Q1, Q3) | 31.4 (24.3, 43.2) |
| Age binary, n (%) |  |
| <30y | 1417 (45.2%) |
| ≥30y | 1721 (54.8%) |
|  | HR (95% CI), p-value for 5y PFS |
| Age (continuous) | 1.01 (1.00, 1.02), p=0.07 |
| Age spline |  |
| Age effect <30y | 0.98 (0.91, 1.06), p=0.68 |
| Age effect ≥30y | 1.05 (1.02, 1.07), p<0.01 |

* Maximum tumor diameter for development cohort and relationship with 5y PFS

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|  | Summary Statistics |
| MTD (cm), mean (SD) | 5.5 (3.5) |
| MTD (cm), median (Q1, Q3) | 4.8 (3.0, 7.4) |
| MTD (cm), min, max | 0, 23 |
| MTD binary, n (%) |  |
| ≤15  | 3104 (98.9) |
| >15 | 34 (1.1) |