79.1. Hodgkin and Non-Hodgkin Lymphomas: Diffuse Large B Cell Lymphoma

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Emerging Prognostic Factors for Clinical Care

Tumor Somatic Mutations. One of the factors that might become important is determination of tumor-specific somatic mutations. Its value recently was demonstrated in elucidating our understanding of the response of ABC-DLBCL to ibrutinib.[1] Activating mutation of CARD11, which is downstream of BTK, the target of ibrutinib, predicted lack of activity, whereas activating mutation of CD79b, upstream of BTK, was associated with enhanced activity of ibrutinib as a single agent. However, evaluation of somatic mutation cannot be recommended as a necessary component of care without additional data.

TABLE 79.3. DLBCL emerging factors for clinical care

Factor	*Definition*	*Clinical significance*	*Level of evidence*
Tumor somatic mutations[1]	Identification of specific gene mutations by targeted sequencing	Mutations in specific genes may provide basis for sensitivity or resistance to treatment: e.g., CARD11 mutation in ABC-DLBCL predicts resistance to ibrutinib.	III

Risk Assessment Models

Risk assessment models and prognostic tools play an important role in cancer medicine because they provide a mechanism to integrate disparate data elements into a process that leads to decreased prognostic heterogeneity. Such processes are useful for (1) identifying and characterizing important prognostic factors, (2) improving prognostic predictions for individual patients, and (3) designing, conducting, and analyzing clinical trials.[2] The most common type of prognostic tool is a prognostic calculator that provides time-specific outcome (e.g., 5-year OS) probability predictions for individual patients based on their demographic, clinical, and tumor characteristics. The prognostic nomogram developed by Yang et al[3] is an example of a risk calculator. Another type of prognostic tool is a prognostic classifier that places patients into ordered prognostic risk classes (either directly or based on cutoffs for individual probability estimates). The remaining tools referenced in this chapter (e.g., IPI, MIPI, FLIPI, and CLL-IPI) are prognostic classifiers. The AJCC Precision Medicine Core (PMC) developed

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and published criteria for critical evaluation of prognostic calculators,[4] which are presented and discussed in Chapter 4. The prognostic nomogram developed by Yang et al[3] meets all but one of the AJCC PMC criteria because it lacks discussion of how missing data were treated.

Recommendations for Clinical Trial Stratification

The authors have not provided any recommendations for clinical trial stratification at this time.

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