**Aggressive B-cell Lymphoma Diagnostic Algorithm**

**Morphology:** diffuse large B-cell lymphoma (DLBCL), high grade B-cell lymphoma (HGBCL), or Burkitt lymphoma

- **Positive for MYC rearrangement but negative for IGH/MYC fusion**
  - FISH: BCL2 and BCL6 BAP
  - Add IGK/MYC and IGL/MYC D-FISH only if pediatric patient and/or high suspicion for Burkitt lymphoma

- **Negative for BCL2 and BCL6 rearrangements**
  - Morphology: DLBCL vs HGBCL vs Burkitt lymphoma
  - HGBCL vs Burkitt lymphoma
  - DLBCL

- **Positive for BCL2 and/or BCL6 rearrangements**
  - Morphology: DLBCL vs HGBCL
  - High-grade B-cell lymphoma, with MYC and BCL2 and/or BCL6 rearrangements
  - Cell of origin (COO) immunohistochemistry (IHC) (CD10, BCL6, MUM1) and double expresser IHC (BCL2 and MYC)

**BLYMF / B-Cell Lymphoma, FISH, Tissue**

- MYC break-apart FISH probe (BAP) and IGH/MYC dual fusion FISH (D-FISH) probe

**Negative for MYC rearrangement and negative for IGH/MYC fusion**

- Burlat lymphoma likely excluded, however,
  - Consider CMAPT / Chromosomal Microarray, Tumor, Formalin-Fixed Paraffin-Embedded for 11q23 aberrancy and 11q24-ter deletion
  - Consider D-FISH for IGK/ MYC and IGL/MYC to exclude a MYC rearrangement completely, especially in a pediatric patient