Aggressive B-cell Lymphoma
Diagnostic Algorithm

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

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

**MYC** rearrangement and/or positive 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

**MYC** rearrangement but negative for IGH/MYC fusion

**MYC** rearrangement and/or positive for IGH/MYC fusion

**BCL2 and BCL6** rearrangements

**HGBCL** vs Burkitt lymphoma

**COO IHC:** CD10, BCL6, MUM1
**Double expresser IHC** (BCL2 and MYC)

**BCL2+ and MYC+**

**BCL2 and MYC**

**Non-germinal center B-cell phenotype**

**Germinall center B-cell phenotype**

**MUM1**

**Non-germinal center B-cell phenotype**

**Germinall center B-cell phenotype**

**Burkitt lymphoma likely excluded, however,**
- **Consider CMA**
- **Consider D-FISH for IGK/MYC and IGL/MYC to exclude a MYC rearrangement completely, especially in a pediatric patient**

**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)**

**BCL2** and **BCL6** rearrangements

**HGBCL** vs HGBCL vs Burkitt lymphoma

**IHC:** CD10, CD43, BCL2, BCL6, MUM1, MYC

**Any other phenotype**

**COO IHC (CD10, BCL6, MUM1)**

**POSITIVE**

**NEGATIVE**

**BCL2** and **MYC**

**BCL6**

**Double expresser**

**Not a double expresser**

**All others**

**COO IHC: CD10**

**Double expresser IHC:** BCL2 and MYC

**All others**

**BCL2+ and MYC+**

**HGBCL, not otherwise specified**

**DLBCL**

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

**Negative for BCL2 and BCL6 rearrangements**

**FISH:** BCL2 and BCL6 BAP.

**Morphology:** DLBCL vs HGBCL

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

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

**Non-germinal center B-cell phenotype**

**CD10+, CD43+, BCL2+, BCL6+, MUM1+, MYC+, BCL2–**

**Probably Burkitt lymphoma, particularly if IG/MYC identified. Confirm with morphology and clinical.**

**HGBCL, not otherwise specified**

**Possible Burkitt lymphoma**

**HGBCL vs Burkitt lymphoma**

**Any other phenotype**

**BCL2+ and MYC+**

**All others**

**Not a double expresser**

**Double expresser**

**BCL2** and **MYC**