Common Targeted Therapies

Drug	Mechanism	Used In	Pharma/ Metabolism/ Excretion	Side Effects		Antidote/ Co-Treatment	Pharmaco-genomic Biomarkers
				Short-Term	Long-Term		
Crizotinib	Inhibitor of ALK, ROS1, and NTRK1 kinases	Lymphoma NBL Others	Liver	Nausea Vomiting Diarrhea	-	-	Mutation or fusion of ALK, ROS1, NTRK1
Rituximab	Monoclonal antibody against CD20 (B-cell lineage marker)	ALL Lymphoma	-	Infusion reactions Cytokine release syndrome Pulmonary toxicity	Reactivation of viruses	-	-
Dinutuximab (ch14.18)	Monoclonal antibody against GD2 glycolipid	NBL	-	Capillary leak syndrome Hypotension Neuropathic pain Hyper-sensitivity reactions	-	-	-
Chimeric antigen receptor (CAR) T cells	Engineered patient T cells expressing modified CD19 receptors, which kill B-lineage cells	B-ALL	-	Cytokine release syndrome (fevers, myalgias, capillary leak/ hypotension, resp. failure) Encephalo-pathy	B cell aplasia	Tocilizumab (IL6R antagonist) for severe CRS	-

Oncologic Emergencies

Tumor Lysis Syndrome (TLS)

Definition	• An oncologic emergency that is caused by massive tumor cell lysis and the release of large amounts of intracellular contents (**potassium, phosphate, and uric acid**) into the systemic circulation • Most often occurs after the initiation of cytotoxic therapy in patients with high-grade lymphomas (particularly the Burkitt subtype) and ALL • Can also occur spontaneously and with other tumor types that have a high proliferative rate, large tumor burden, or high sensitivity to cytotoxic therapy
Pathogenesis	• Rapid lysis of tumor cells releases large amounts of intracellular contents (potassium, phosphate, and nucleic acids) into circulation leading to hyperkalemia, hyperphosphatemia, secondary hypocalcemia, hyperuricemia. • Purines are metabolized to hypoxanthine and xanthine, and then to uric acid via xanthine oxidase. • Uric acid is poorly soluble in water leading to crystal precipitation and deposition in the renal tubules and AKI. • Allopurinol competitively inhibits xanthine oxidase, blocking the metabolism of hypoxanthine and xanthine to uric acid. Xanthine is less soluble than uric acid so allopurinol can exacerbate AKI. • Cancer cells have ~4X higher Phos than normal cells. Hyperphosphatemia can lead to secondary hypocalcemia and renal calcium phosphate precipitation. Hypocalcemia may also cause cardiac arrhythmias. • Elevated uric acid and phosphate worsen the severity of AKI (increases precipitation of each other)

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