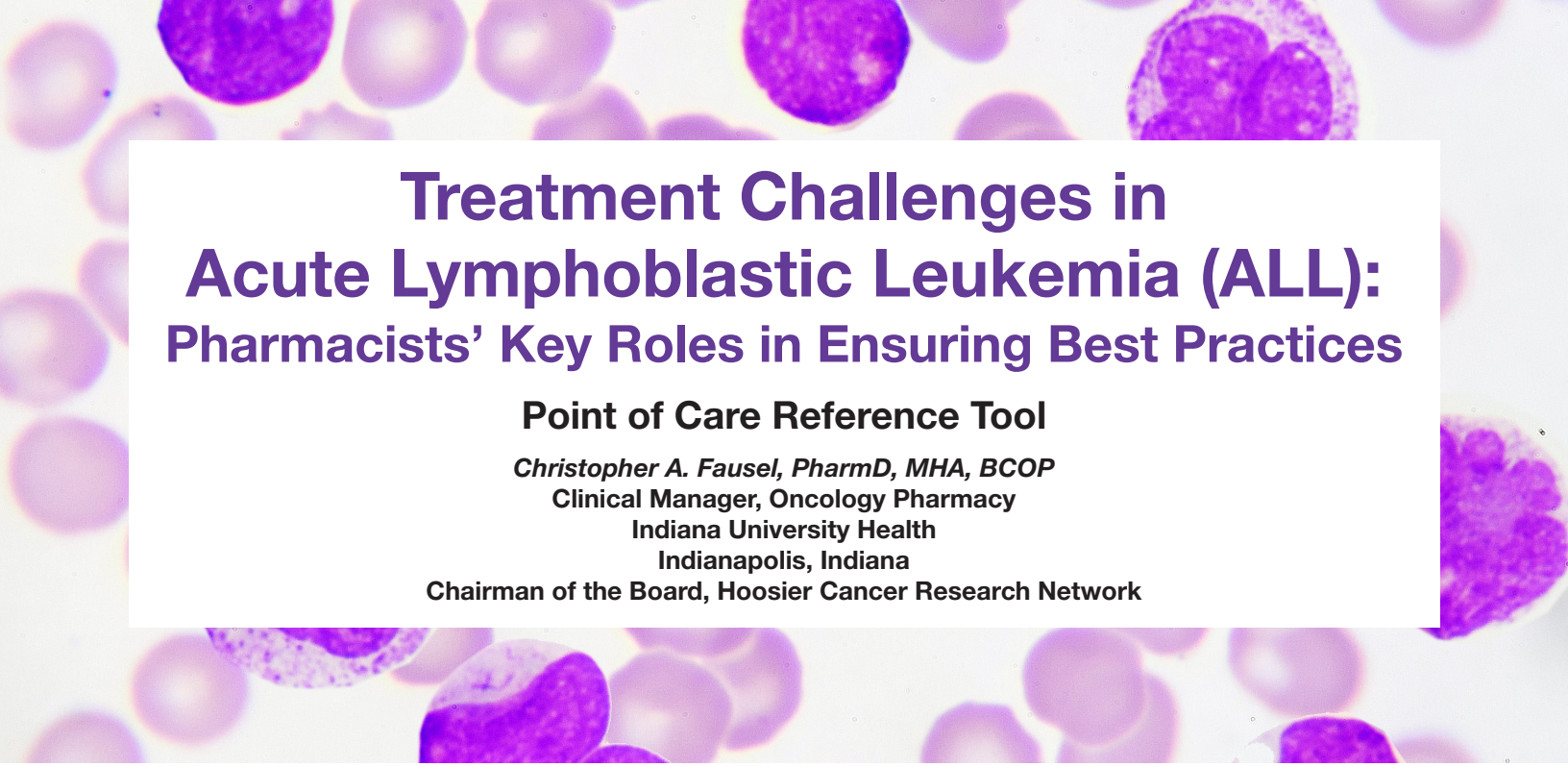

Treatment Challenges in Acute Lymphoblastic Leukemia (ALL):

Pharmacists' Key Roles in Ensuring Best Practices

Point of Care Reference Tool

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Vincristine Sulfate Liposomal Injection (VSLI)

Dosing	**2.25 mg/m^2 IV over 1 hour once every 7 days**
FDA-labeled indication	Treatment of adult patients with Ph- ALL in second or greater relapse or whose disease has progressed following 2 or more antileukemic therapies. *This indication is based on overall response rate. Clinical benefit such as improvement in overall survival has not been verified.*
Pharmacy preparation notes	Requires vincristine/sodium phosphate/sphingomyelin cholesterol liposome to be heated in a water bath (Prep time: 60 to 90 minutes)
Monitoring parameters	Medication safety – intrathecal injection/drug name Neuropathy/constipation/SIADH Hepatotoxicity Extravasation risk Tumor lysis syndrome
Drug interactions	CYP 3A4/5 inhibitors and inducers P-glycoprotein inhibitors

Abbreviations: ALL, acute lymphoblastic leukemia; CYP, cytochrome P450; FDA, United States Food and Drug Administration; IV, intravenously; Ph-, Philadelphia chromosome-negative; SIADH, syndrome of inappropriate antidiuretic hormone secretion.

Blinatumomab

Dosing	**MRD-POSITIVE B-CELL ALL:** **Induction Cycle 1:** Days 1-28: 28 mcg/day* IV Days 29-42: 14 days treatment free **Consolidation Cycles 2 through 4:** Days 1-28: 28 mcg/day* IV Days 2-42: 14 days treatment free **RELAPSED/REFRACTORY ALL:** **Induction Cycle 1:** Days 1-7: 9 mcg/day IV *(for patients who weigh less than 45 kg: 5 mcg/m^2/day dose)* Days 8-28: 28 mcg/day* IV Days 29-42: 14 days treatment free **Induction Cycle 2:** Days 1–28: 28 mcg/day* IV Days 29-42: 14 days treatment free **Consolidation Cycles 3 through 5:** Days 1-28: 28 mcg/day* IV Days 29-42: 14 days treatment free **Consolidation Cycles 6 through 9:** Days 1-28: 28 mcg/day* IV Days 29-84: 56 days treatment free **For patients who weigh less than 45 kg: 15 mcg/m^2/day dose*
FDA-labeled indications	B-cell precursor ALL in first or second remission with MRD greater than or equal to 0.1% Relapsed or refractory B-cell precursor ALL
Pharmacy preparation notes	Continuous infusion – may be prepared for 24-hour, 48-hour, or 7-day bags Solution stabilizer added to NS diluent IV lines primed with diluted drug in NS diluent
Monitoring parameters	CRS Neurotoxicity Tumor lysis syndrome Pancreatitis Leukoencephalopathy Infusion-related reactions
Drug Interactions	Transient release of cytokines that could suppress CYP isoenzymes (particularly during first 9 days of Cycle 1)

Abbreviations: ALL, acute lymphoblastic leukemia; CRS, cytokine release syndrome; CYP, cytochrome P450; FDA, United States Food and Drug Administration; IV, intravenously; MRD, minimal residual disease; NS, normal saline.

Inotuzumab ozogamicin

Dosing	**Cycle 1 (length, 21 days):** Day 1: 0.8 mg/m^2 IV Days 8, 15: 0.5 mg/m^2 IV **Subsequent cycles (length, 28 days):** *If* CR: Days 1, 8, 15: 0.5 mg/m^2 IV *If* no CR: Day 1: 0.8 mg/m^2 IV; Days 8, 15: 0.5mg/m^2 IV
FDA-labeled indication	Treatment of adults with relapsed or refractory B-cell precursor ALL
Pharmacy preparation notes	4-hour expiration following dilution of reconstituted solution (1-hour infusion)
Monitoring parameters	Infusion-related reactions Hepatotoxicity including increased veno-occlussive disease/sinusoidal obstruction syndrome with HSCT Cytoreduction to lower peripheral blast count to < 10,000 mm^3 Hemorrhage
Drug interactions	QT interval prolongation

Abbreviations: ALL, acute lymphoblastic leukemia; CR, complete response; FDA, United States Food and Drug Administration; HSCT, hematopoietic stem cell transplant; IV, intravenously.

Tisagenlecleucel

Dosing	*For patients who weigh more than 50 kg:* 0.1-2.5x10^8 total CAR-positive viable T-cells IV (non-weight based) *For patients who weigh 50 kg or less:* 0.2-5x10^6 CAR-positive viable T-cells per kg of body weight
FDA-labeled indication	Patients up to 25 years of age with B-cell precursor ALL that is refractory or in second or later relapse
Pharmacy preparation notes	1. Patient undergoes apheresis at the treating center to harvest autologous T-cells 2. Cells are shipped to manufacturer facility for transduction with a lentivirus to express a CAR containing a T-cell activation signal that is specific for CD19 3. Cells are shipped from manufacturer lab to institutional stem cell lab for final preparation and patient administration
Monitoring parameters	CRS (administer tocilizumab 8 mg/kg [max dose 800 mg]) Neurotoxicity Toxicities of lymphodepleting chemotherapy (e.g., cyclophosphamide/fludarabine) Hypogammaglobinemia Prolonged cytopenias (> day +28)
Drug-drug interactions	HIV and the lentivirus used to transduce the patient's cells have limited, short spans of identical RNA; commercial HIV nucleic acid tests may yield false positive results

Abbreviations: ALL, acute lymphoblastic leukemia; CAR, chimeric antigen receptor; CRS, cytokine release syndrome; FDA, United States Food and Drug Administration.