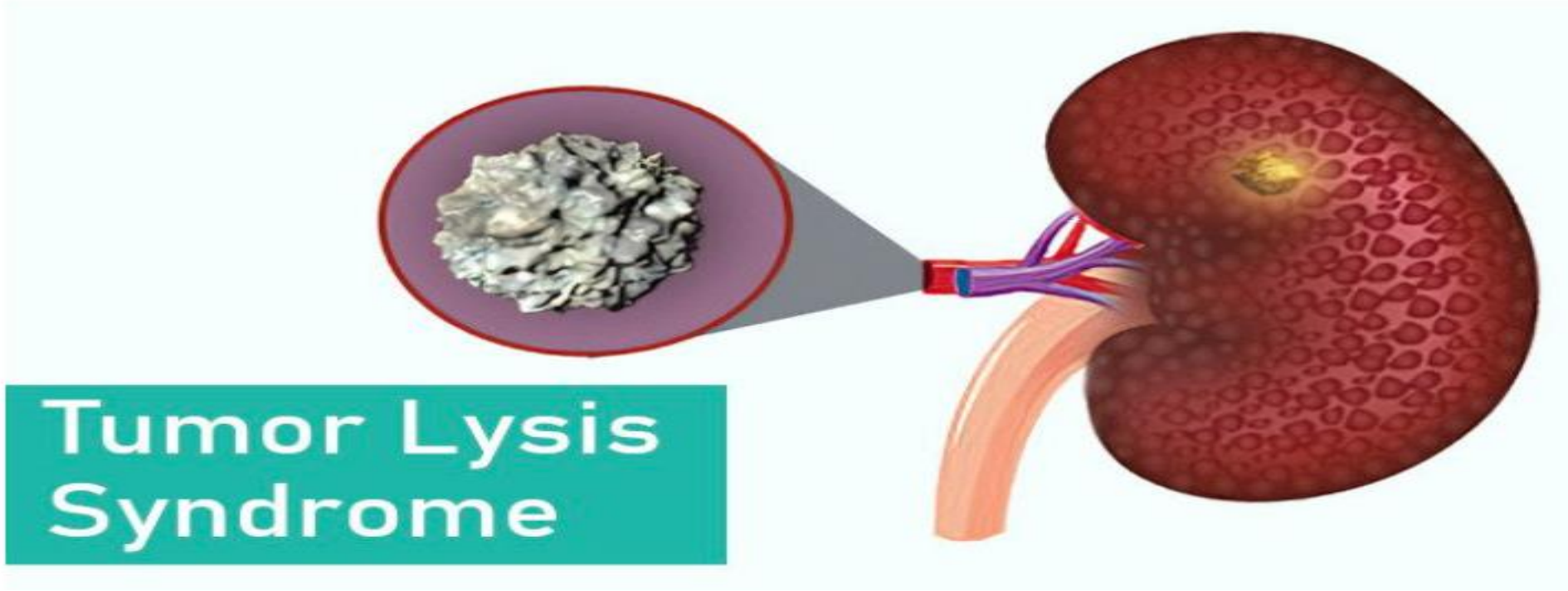
In the name of God

Tumor lysis Syndrome



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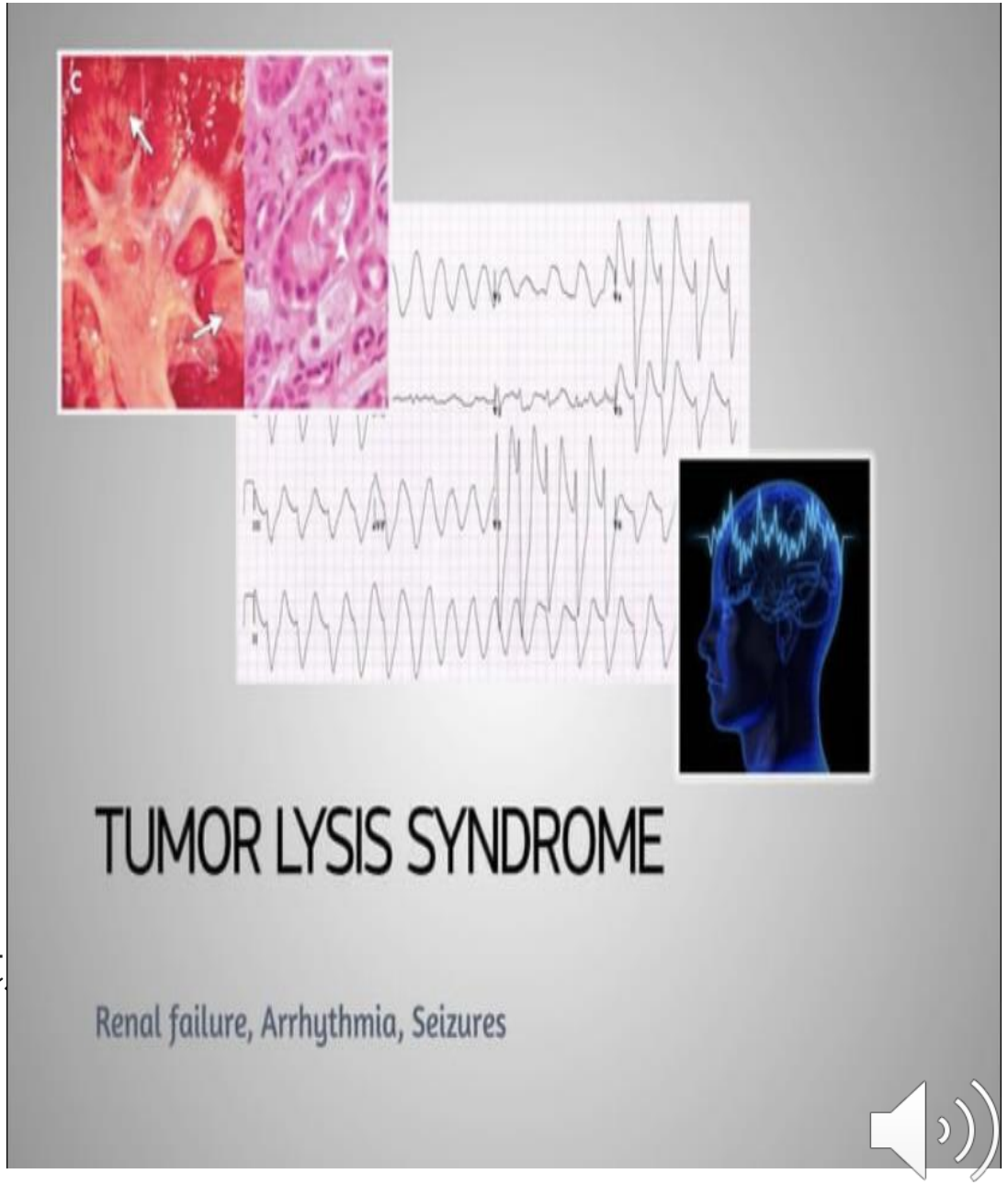
Introduction

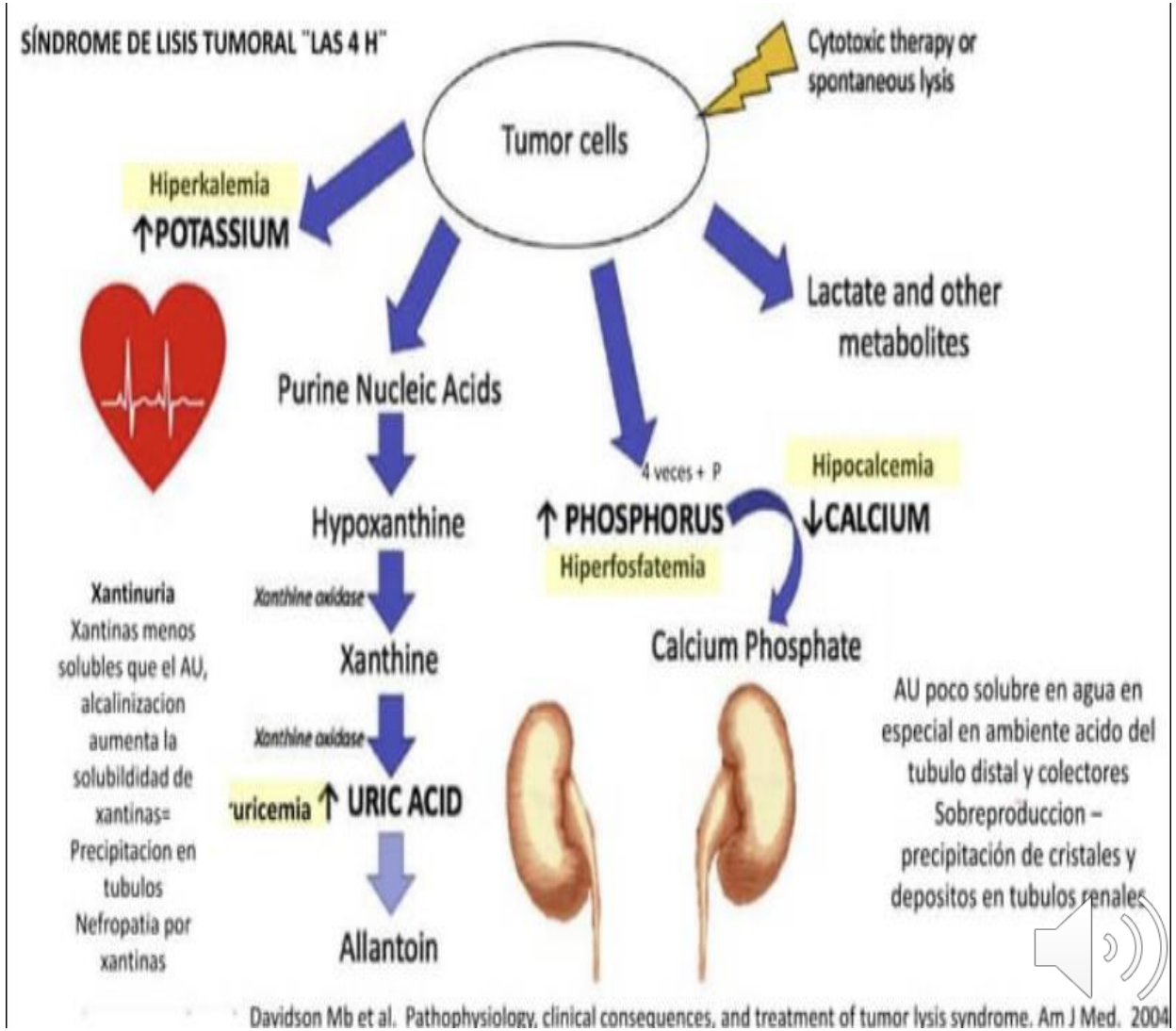
- Tumor lysis syndrome is the most common oncologic emergency.
- This condition is prevalent in both adult and pediatric oncology patients undergoing chemotherapy, though it can also occur spontaneously.
- Most of the symptoms seen in patients with tumor lysis syndrome are related to the release of intracellular chemical substances that cause impairment in the functions of target organs.
- This can lead to acute kidney injury (AKI), fatal arrhythmia, and even death.
- The initiation of treatment for TLS is a medical emergency that must be addressed in a multidisciplinary team (oncologist, nephrologist, critical care physician) in order to reduce the risk of death and that of chronic renal impairment.



Epidemiology

- The precise incidence of tumor lysis syndrome is not known.
- The most common malignancies associated with tumor lysis syndrome include **non-Hodgkin lymphoma (30%), solid tumors (20%), acute myeloid leukemia (19%), and acute lymphocytic leukemia (13%).**

- The overall in-hospital mortality was approximately 21%Cairo *et al.*
- **High-Risk Tumors**
- Acute lymphocytic leukemia (5.2% to 23%)
- Acute myeloid leukemia with a WBC count greater than 75,000 (18 %)
- B-cell acute lymphoblastic leukemia (26.4%)
- Burkitt lymphoma (14.9%)
- **Intermediate-Risk Tumors**
- Acute myeloid leukemia with WBC counts between 25,000 and 50,000 (6%)
- Diffuse large B-cell lymphoma (6%)
- **Low-risk Tumors**
- Acute myeloid leukemia with WBC count less than 25,000 (1%)
- Chronic lymphocytic leukemia (0.33%)
- Chronic myelogenous leukemia (Case reports)
- A solid tumor (Case reports)

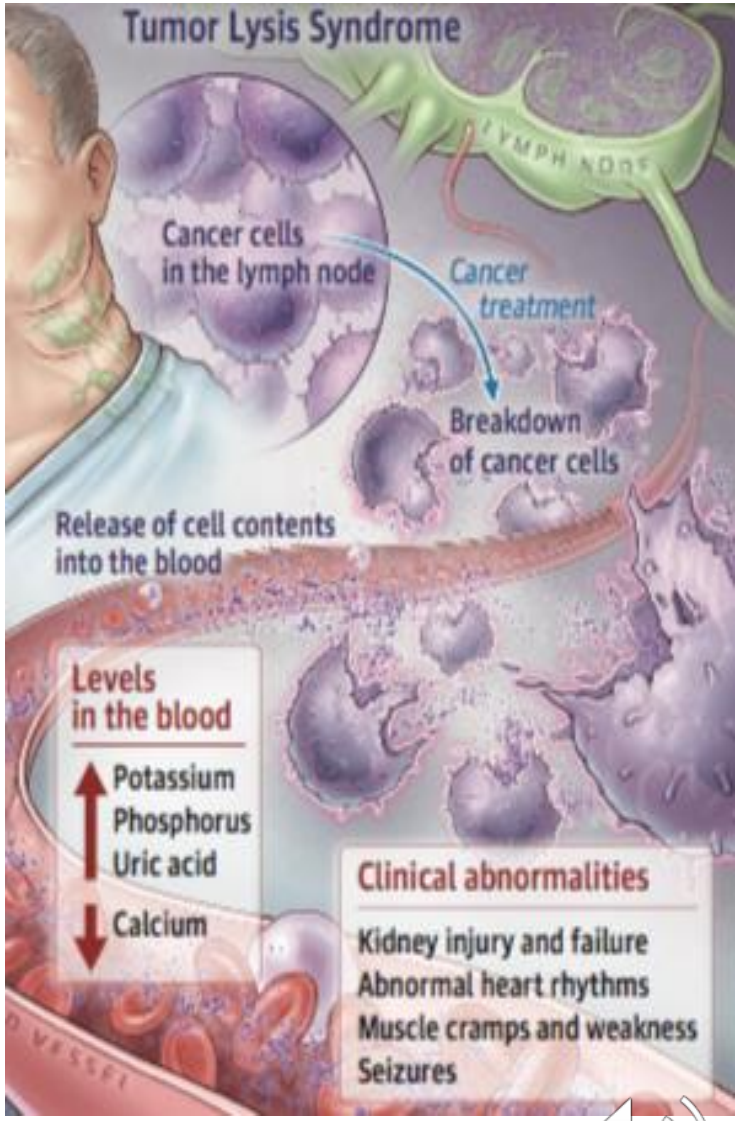


Etiology

- *Patients with huge "tumor burdens" (number of cancer cells in the body) or have rapidly dividing cells that respond well with treatment are at high risk. These include*:
- **Leukaemia**
- **Non-Hodgkin lymphoma**
- **Tumors like hepatoblastoma and neuroblastoma**
- **Myeloproliferative diseases or neoplasm**
- Cancer that causes the ill function of the kidney before the treatment start

- **OTHER RISKS**
- **Intrathecal chemotherapy** (injection of chemotherapy, given directly into the fluid-filled space around the brain and spinal cord).
- **Chemoembolization** (soothing treatment for tumors found in the liver).
- **Radiation therapy** (uses a beam of huge and intense energy to kill cancer cells)
- **Corticosteroid therapy**
- **Hormonal and biological therapy**

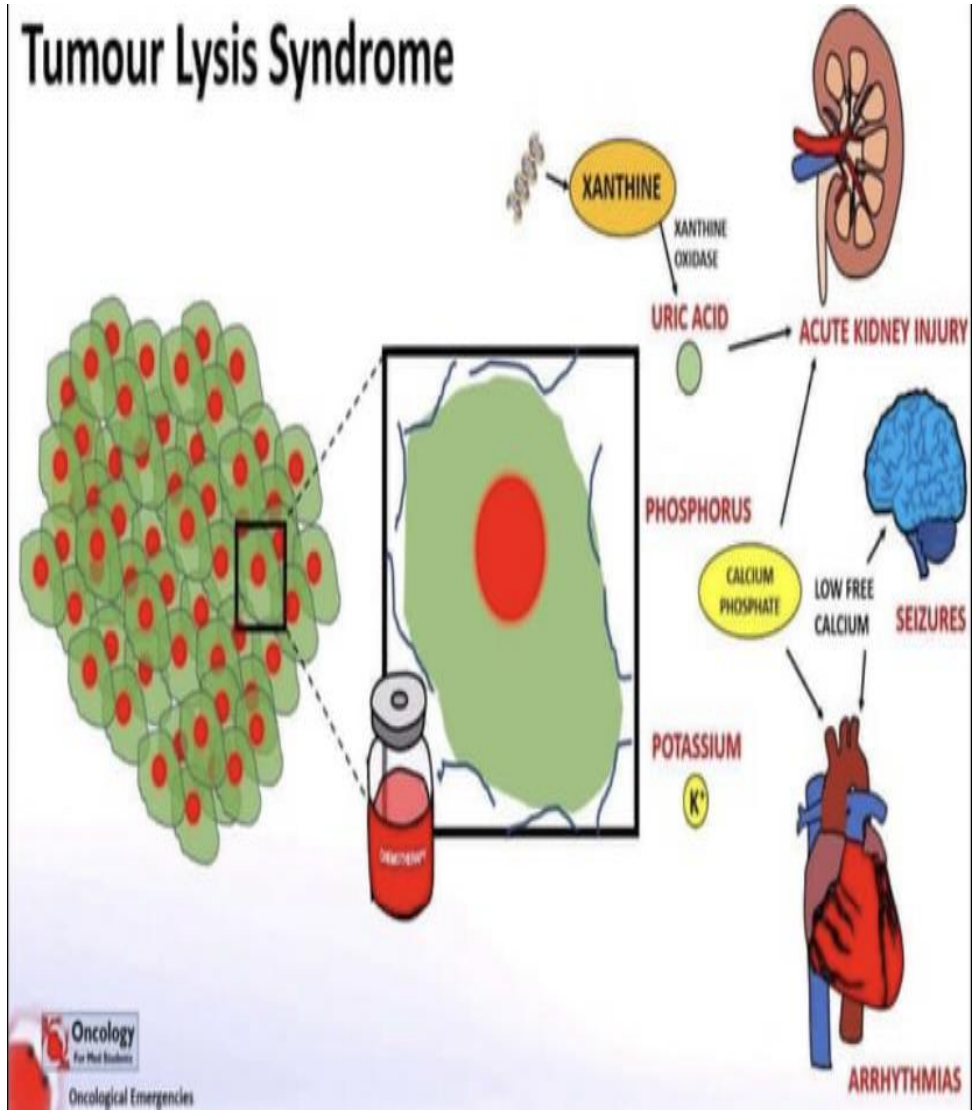
- TLS usually develops within a few hours to 2-3 days after the start of the chemotherapy.
- The mortality rate of patients suffering from tumor lysis syndrome is less the 20%



JAMA Oncology June 2018 Volume 4, Number 6

Others

- Rarely, TLC is associated with the administration of steroids, biological immunomodulators as well as monoclonal antibodies.
- Thalidomide
- Bortezomib
- Hydroxyurea
- Paclitaxel
- Fludarabine
- Etoposide
- Zoledronic acid
- In rare instances, tumor lysis syndrome has been observed in patients under **general anesthesia undergoing surgery**.
- Other rare occurrences of tumor lysis syndrome are seen in **pregnancy or high fever.**



Novel Agents Associated With Tumor Lysis Syndrome

Agent	Class	Treated Malignancies	Observed TLS Incidence Single-Agent/Combination Therapy
Monoclonal antibodies			
Brentuximab	Anti-CD30 and antimicrotubular agent (monomethyl auristatin E)	ALCL	1.7%
Cituximab	EGFR inhibitor	Metastatic colon carcinoma	Case reports
Obinutuzumab	Anti-CD20	CLL, NHL, relapsed/refractory DLBCL	3%–5%
Ofatumumab	Anti-CD20	Relapsed/refractory DLBCL, relapsed CLL	0%/0% grades 3–4 TLS (with lenalidomide)
Rituximab	Anti-CD20	Indolent and aggressive NHLs, PTLD	Low incidence in case reports and case series
Kinase inhibitors			
Alvocidib (flavopiridol)	CDK inhibitor	AML	4.2%/42.2%
Dasatinib	Bcr-Abl and Src TKI	Chronic/accelerated/blast phase CML, Ph^+ ALL	3.4%/4.2%
Dinaciclib	CDK inhibitor	ALL, AML, relapsed/refractory CLL	15%
Ibrutinib	Bruton TKI	CLL/SLL	0%/6.7%
Idelalisib	Small-molecule inhibitor of PI3K	Refractory/relapsed MCL and CLL, previously treated indolent NHL	0%
Imatinib	Bcr-Abl TKI	Chronic/blast phase CML, Ph^+ ALL, metastatic GIST	Case reports
Nilotinib	Bcr-Abl TKI	Accelerated phase CML	Case reports
Sorafinib	VEGFR TKIs	HCC, RCC	Case reports
Sunitinib	VEGFR TKIs	GIST, RCC	Case reports

Novel Agents Associated With Tumor Lysis Syndrome

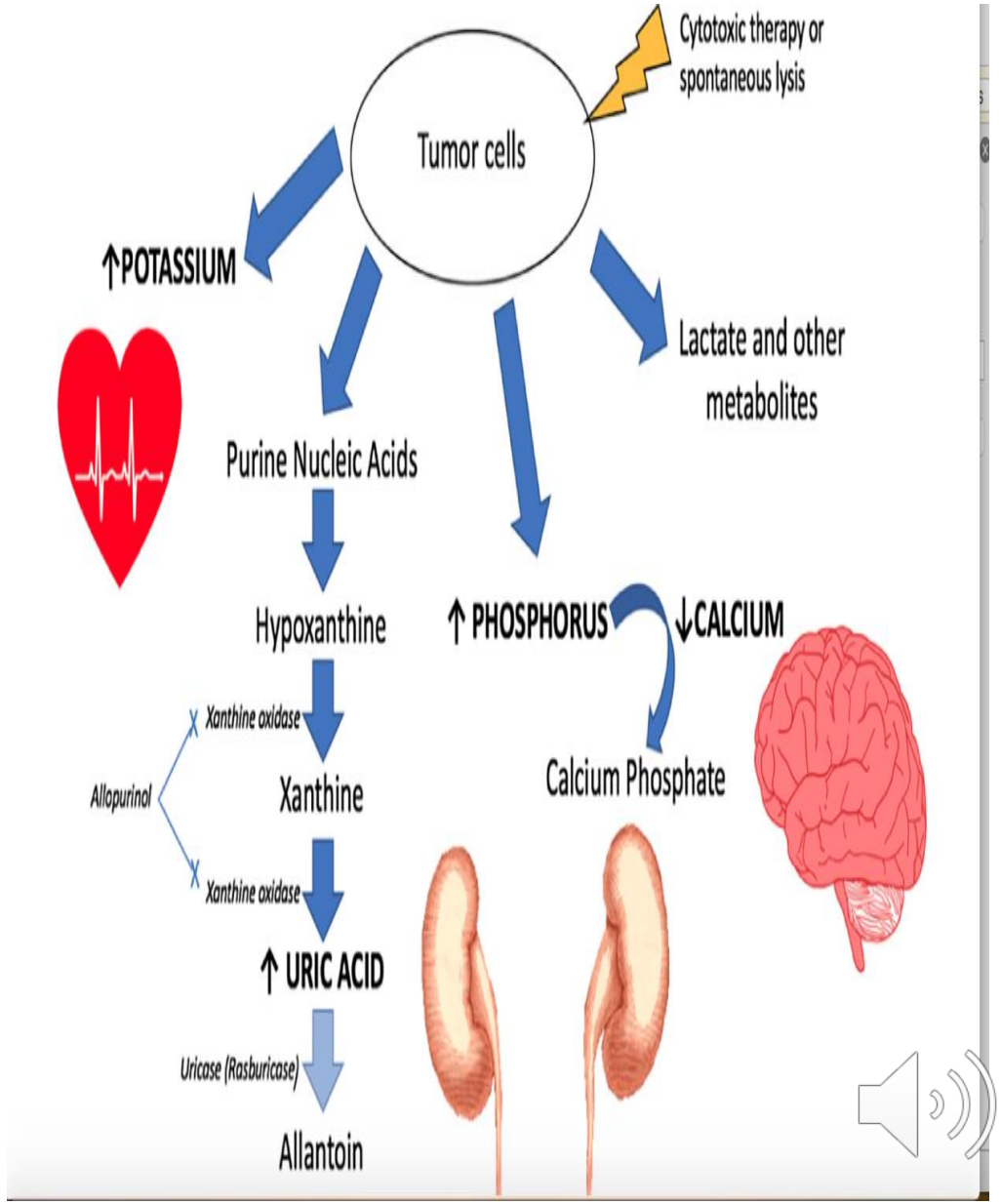
Chimeric immunoreceptors			
CAR-T	CD19 targeted	Persistent B-cell malignancies after allogeneic HCT	10%
Proteasome inhibitors			
Bortezomib	Reversible proteasome inhibitor	MM	1.4%–5% (±dexamethasone)
Carfilzomib	Irreversible proteasome inhibitor	Relapsed/refractory MM	0.4%–4.3%
Oprozomib	Structural analog of carfilzomib	MM, Waldenström macroglobulinemia	2.4%
Immunomodulatory agents			
Lenalidomide	Analog of thalidomide	CLL (initial therapy), relapsed/refractory CLL or NHL	0%–4%/1.7% with rituximab
Thalidomide	Unknown mechanism of action	MM, HCC	Case reports
Bcl-2 inhibitors			
Venetoclax	Small-molecule Bcl-2 inhibitor	Relapsed/refractory CLL	3.2%–8.9% (2 fatalities)/2.7% (fatality) with rituximab

CLINICAL FEATURES

- Tumor lysis syndrome generally occurs within 12 to 72 hours following the initiation of cytotoxic therapy, although manifestations arise infrequently prior to receiving therapy—called spontaneous TLS—or may extend beyond 72 hours after treatment initiation.

- Symptoms reflect the underlying metabolic abnormalities and may include nausea, vomiting, diarrhea, anorexia, weakness, lethargy, hematuria, cardiac dysrhythmias, seizures, muscle cramps, tetany, and syncope.

- Changes in blood levels of uric acid, potassium, phosphorus, and calcium can affect the functioning of several organs, especially the kidneys, and also the heart, brain, muscles, and gastrointestinal tract.



Arch Pathol Lab Med (2019) 143 (3): 386–393.

Risk Factors for the Tumor Lysis Syndrome

CATEGORIES OF RISK FACTORS

1.CANCER MASS:-

- Bulky tumor or extensive metastasis
- Organ infiltration by cancer cells
- Bone marrow involvement
- Renal infiltration or outflow-tract obstruction

2. CELL LYSIS POTENTIAL:-

- High rate of proliferation of cancer cells
- Cancer-cell sensitivity to anticancer therapy
- Intensity of initial anticancer therapy

3. FEATURES ON PATIENT PRESENTATION

- Nephropathy before diagnosis of cancer
- Dehydration or volume depletion
- Acidic urine
- Hypotension
- Exposure to nephrotoxins

4. SUPPORTIVE CARE

- Inadequate hydration
- Exogenous potassium
- Exogenous phosphate
- Delayed uric acid removal

Epidemiology & Prognosis

Cancer Mass

- Bulky or metastatic
- Organ involvement

Lysis Potential

- Proliferation Rate
- Cell Sensitivity
- Chemo Intensity

Patient Factors

- Renal Impairment
- Hypotension/ Volume depletion
- Nephrotoxins

TLS ↑ Risk of death during treatment and ↑ LOS

Risk Factors for Tumor Lysis Syndrome

- Disease-related factors
  - Rapid cellular proliferation rate
    - Elevated serum LDH (>2 times the ULN)
  - High tumor burden
    - Bulky tumors (>10 cm)
    - Widely metastatic disease
    - Elevated WBC count (>25 × $10^3/\mu L$)
  - Sensitivity to cytoreductive therapy
  - Renal infiltration or outflow tract obstruction by tumor
- Patient-related factors
  - Preexisting renal disease/uremia
    - Nephropathy
    - Renal failure or oliguria
    - Urinary tract obstruction
  - Pretreatment hyperuricemia or hyperphosphatemia
  - Hypovolemia or hypotension
  - Acidic urine
- Treatment-related factors
  - Intensity of cytoreductive therapy
    - Single-agent versus combination therapy
    - Disease-specific, varies according to tumor type
  - Inadequate hydration during cytoreductive therapy

https://doi.org/10.5858/arpa.2017-0278-RS

Risk of developing tumor lysis syndrome

High-Risk Tumors

- Advanced Burkitt lymphoma
- Advanced leukemia
- Early-stage leukemia or Burkitt lymphoma with elevated lactate dehydrogenase
- Acute lymphocytic leukemia with a white cell count of more than 100,000/microliters, or if the increase of lactate dehydrogenase from the baseline is two times the upper limit of normal
- Diffuse large B-cell lymphoma (DLBCL) and bulky disease with a baseline lactate dehydrogenase two times the upper limit of normal
- Acute myeloid leukemia (AML) with a white cell count more than or equal to 10,000/microliters

- **Intermediate-Risk Tumors**
- AML with A white cell count between 25,000 and 100,000/microliters
- Acute lymphocytic leukemia (ALL) with a white cell count of less than 100,000/micro L and LDH of less than twice the upper limit of normal
- DLBCL with a baseline increase in lactate dehydrogenase of twice the upper limit of normal but the non-bulky disease
- Early-stage leukemia and Burkitt lymphoma with a lactate dehydrogenase of less than twice the upper limit of normal

- **Low-Risk Tumors**
- Solid cancers
- Multiple myelomas
- Indolent lymphomas
- Chronic lymphocytic leukemia
- Chronic myeloid leukemia
- AML with a WBC count of less than 25,000/microliters and a lactate dehydrogenase elevated to less than two times the upper limit of normal

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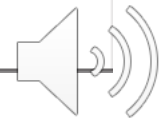
DEFINITION

Cairo–Bishop Definition of Tumor Lysis Syndrome			
Laboratory TLS = modification of at least 2 parameters within 24 h	- Uric acid ≥ 8 mg/dL - Potassium ≥ 6 mg/dL - Phosphate ≥ 4.5 mg/dL	Or 25% increase	within 3 to 7 days after chemotherapy initiation
	- Calcium ≤ 7 mg/dL	Or 25% decrease	
Clinical TLS = laboratory TLS + 1 organ dysfunction or death	- Renal dysfunction (creatinine > 1.5 X normal values) - Cardiac involvement (arrhythmias) - Neurological involvement (seizures, tetany) - Death		

Arch Pathol Lab Med (2019) 143 (3): 386–393.

Cairo-Bishop Grading of Clinical Tumor Lysis Syndrome (TLS)

Complication	Grade 0	1	2	3	4	5
LTLS	Absent	Present	Present	Present	Present	Present
Creatinine[b,c]	<1.5 times the ULN	1.5 times the ULN	>1.5 to 3.0 times the ULN	>3.0 to 6.0 times the ULN	>6.0 times the ULN	Death[d]
Cardiac arrhythmia[b]	None	Intervention not indicated	Nonurgent medical intervention indicated	Symptomatic and incompletely controlled medically; controlled with device (eg, defibrillator)	Life-threatening (eg, associated with CHF, hypotension, syncope, shock)	Death[d]
Seizure[b]	None	Not applicable	One brief, generalized seizure; seizure(s) well controlled by anticonvulsants; infrequent focal motor seizures not interfering with ADL	Seizure in which consciousness is altered; poorly controlled seizure disorder; with breakthrough generalized seizures despite medical intervention	Any prolonged, repetitive, or difficult-to-control seizure (eg, status epilepticus, intractable epilepsy)	Death[d]



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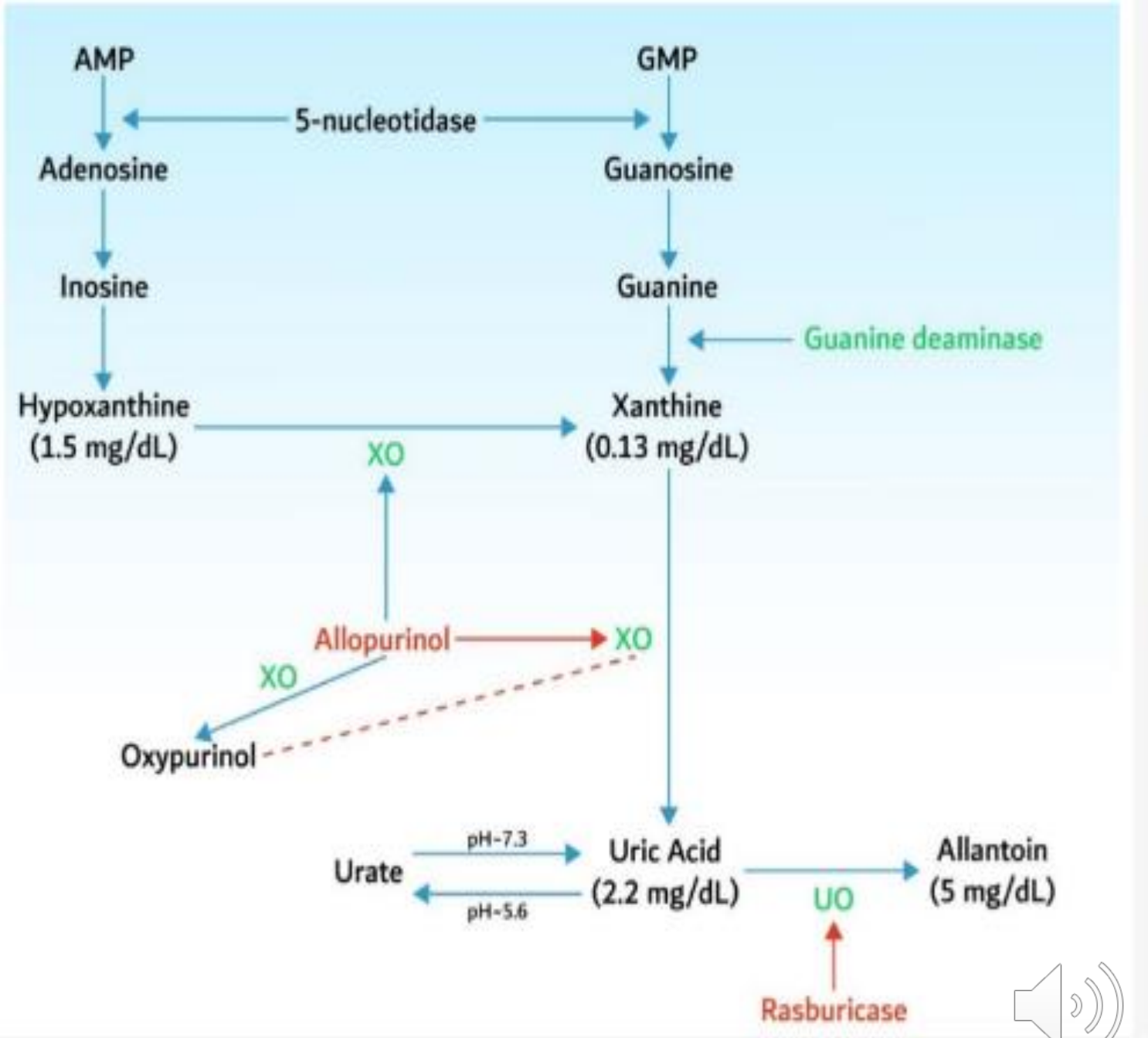
Pathogenesis

The metabolism of the purines adenine and guanine in a stepwise process leads to the production of xanthine.

Nucleic acids (adenosine monophosphate—AMP, guanosine monophosphate—GMP) are metabolized into adenine and guanine and then to hypoxanthine and xanthine, which is finally converted into uric acid under the influence of xanthine oxidase.

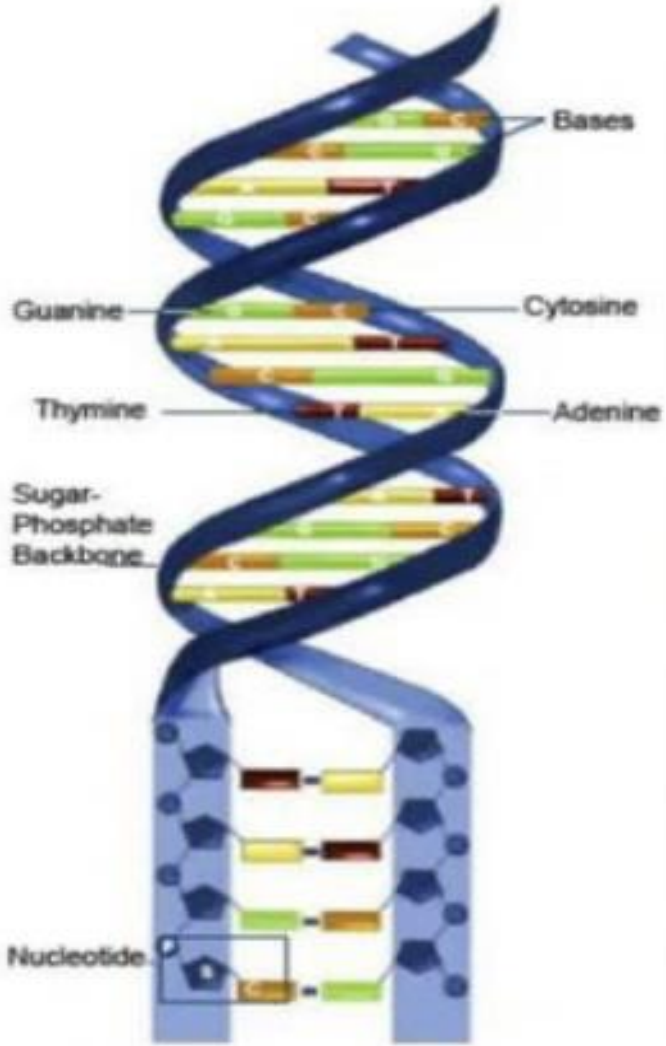
In mammals, uric acid is further metabolized into allantoin (a molecule 5 to 10 times more soluble than uric acid) that is excreted by the kidneys.

This catabolic pathway needs the presence of urate oxidase (OU), an enzyme lacking in humans and higher primates



Biomedicines **2022**, *10*(5), 1012; https://doi.org/10.3390/biomedicines10051012

Complication of Tumor Lysis Syndrome



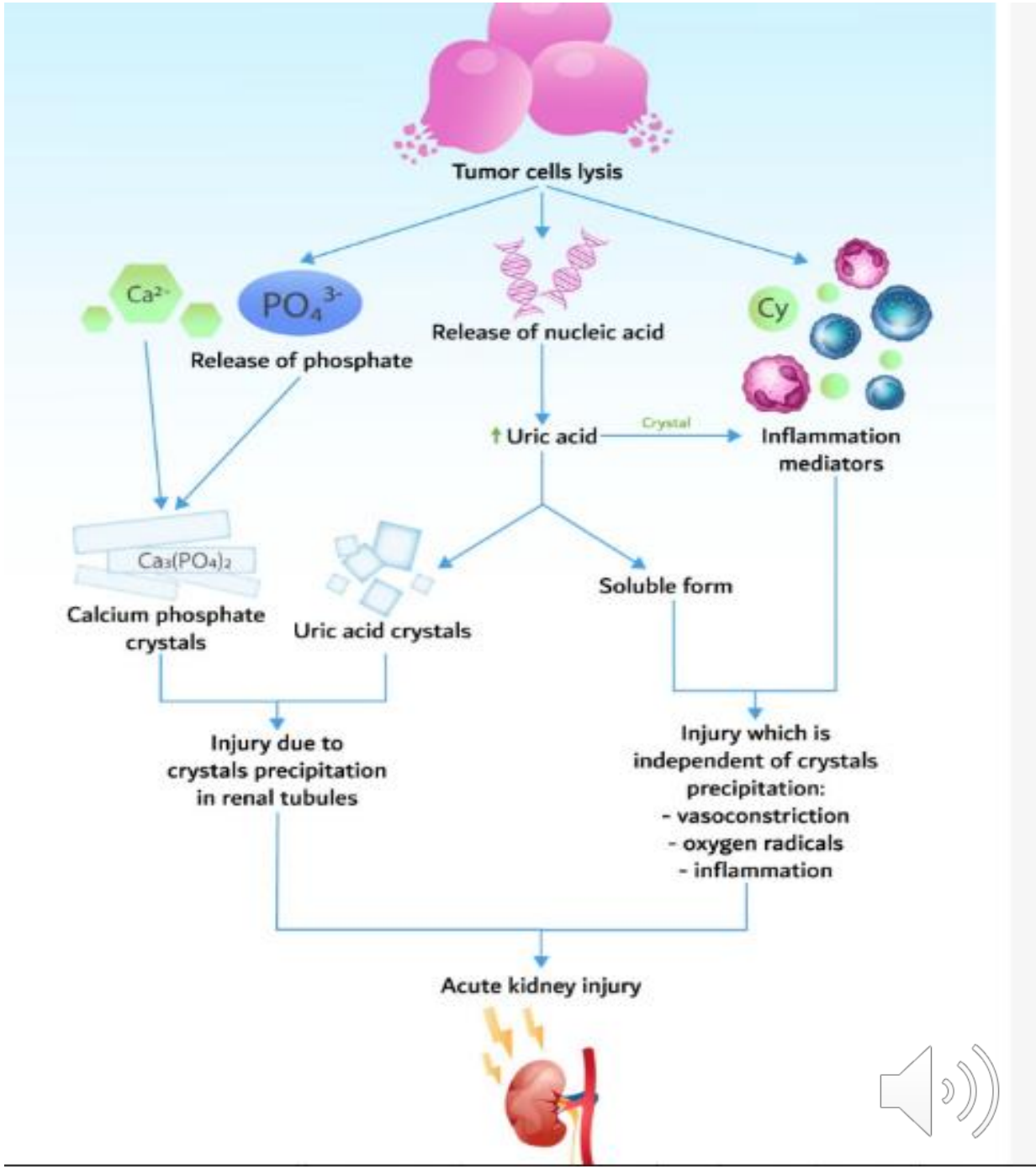
Cell Lysis	• ↑K	Fatal dysrhythmias
DNA Breakdown	• ↑Uric Acid	Renal failure
DNA Breakdown	• ↑PO_4	Renal failure
Ca complexing with PO_4	• ↓Ca	Tetany, dysrhythmia, renal failure
Cytokine release		Multi-organ failure

Howard et al., NEJM, 201

AKI

- An overwhelming production of uric acid is caused crystallization in the renal tubules causing **obstructive uropathy and decreased glomerular filtration rate.**
- Peritubular capillary pressure and vascular resistance also increase.
- The scavenging of nitric oxide produces **vasoconstriction** and **kidney ischemia**.
- Uric acid is also a potential **pro-inflammatory agent** and can cause the release of other cytokine-like tumor necrosis factor-alpha, protein I.
- These cytokines attract white blood cells and facilitate further injury to the kidney.

- The factors that favor the formation of crystals include low urine flow, low solubility, and high levels of solutes.
- The histopathological findings in tumor lysis syndrome are associated with the deposition of **uric acid, calcium phosphate, and xanthine in the lamina of the distal kidney tubules.**



Treatment Strategies

Prevention

Evaluate risk factors

1) Tumor burden
2) Sensitivity
3) Underlying dysfunction

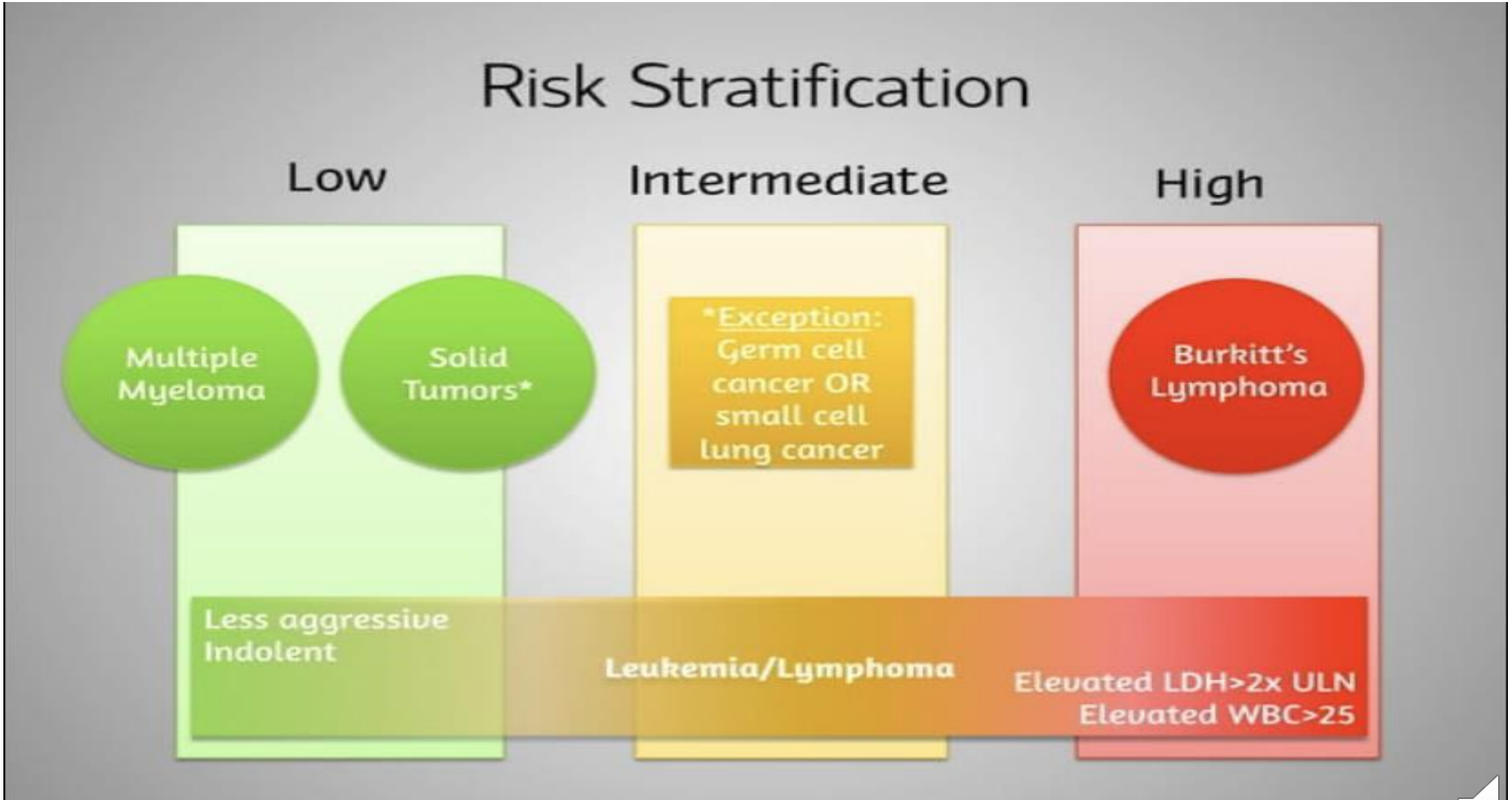
Determine need and INTENSITY of prophylaxis

Treatment

Manage lab abnormalities

- Hyperkalemia
- Hyperphosphatemia
- Hyperuricemia

Dose adjust medications based on renal function


Risk Stratification
Low
Intermediate
High
Multiple Myeloma
Solid Tumors*
*Exception: Germ cell cancer OR small cell lung cancer
Burkitt's Lymphoma
Less aggressive Indolent
Leukemia/Lymphoma
Elevated LDH>2x ULN
Elevated WBC>25

Risk Assessment and Recommended Prophylaxis

Cancer Type	High Risk (TLS Risk >5%)	Intermediate Risk (TLS Risk 1%–5%)[b]	Low Risk (TLS Risk <1%)[c]
Lymphomas and acute leukemias			
Lymphomas	Burkitt or lymphoblastic lymphoma Advanced stage or Early stage and LDH ≥2 times the ULN	Burkitt or lymphoblastic lymphoma Early stage and LDH <2 times the ULN	Cutaneous T-cell lymphoma Follicular lymphoma Hodgkin lymphoma MALT lymphoma Mantle cell lymphoma (nonblastoid variant) Marginal zone lymphoma Small lymphocytic lymphoma
ALL	WBC ≥100 × 10^3/μL or LDH ≥2 times the ULN	WBC <100 × 10^3/μL and LDH <2 times the ULN	
AML	WBC ≥100 × 10^3/μL	WBC 25 to <100 × 10^3/μL or LDH ≥2 times the ULN	WBC <25 × 10^3/μL and LDH <2 times the ULN
Other lymphomas (categorized by age and disease stage)			
Anaplastic large cell lymphoma		Children with advanced stage	Children with early stage Adults
ATL, DLBCL, mantle cell lymphoma (blastoid variant), peripheral T-cell lymphoma, and transformed lymphoma	Children with stage III or IV and LDH ≥2 times the ULN Adults with bulky disease and LDH >ULN	Children with stage III or IV and LDH <2 times the ULN Adults with nonbulky disease and LDH >ULN	Children with stage I or II Adults with normal LDH
Chronic leukemias, myeloma, and solid tumors			
CML			Chronic phase
CLL		Treatment using targeted and/or biologic therapies	
Myeloma			Myeloma
Solid tumors		Chemosensitive bulky solid tumors (eg, germ cell tumors, neuroblastoma, SCLC)	Solid tumors not meeting criteria for intermediate risk
Prophylaxis recommendations	Monitoring Hydration Rasburicase[d]	Monitoring Hydration Allopurinol or rasburicase[d,e]	Monitoring Hydration Consider allopurinol[f]

Prevention

Low risk	Adequate hydration Urine output goals listed Monitor for signs and symptoms of TLS Low threshold for intravenous fluids Consider allopurinol on individual basis
Intermediate risk	Aggressive hydration + allopurinol prophylaxis (or febuxostat) up to 7 days Urine output goals listed Monitor for signs and symptoms of TLS (starting 8 h after treatment initiation, laboratory tests every 8–12 h)
High risk	Aggressive hydration + rasburicase prophylaxis Urine output goals listed Monitor for signs and symptoms of TLS (starting 4–6 h after treatment initiation, laboratory tests every 6–8 h) Consider "preventive" admission to intensive care unit, especially in case of pre-existing cardiac or renal dysfunction

Volume Expansion

- Volume expansion is accomplished by crystalloids solutions, which increase the urine output and thus the phosphate, potassium, and uric acid excretion.
- It is recommended to administer 2500–3500 mL/m^2/day to children (200 mL/kg/day for those whose weight is under 10 kg) and 3000 mL/day to adults by mouth or intravenously for 2 to 3 days before chemotherapy.

- The urine output that should be obtained is
- over 100 mL/m^2/h or a diuresis of 2.5 L/day for adults;
- over 4 mL/kg/h for children.

Diuretics

Diuretics are not routinely recommended because they induce volume depletion, thus compromising the renal hemodynamics even more.

Diuretics are used only in the case of symptomatic hypervolemia.

The loop diuretics are preferred, because, in addition to increasing the urinary flow, they also increase the potassium secretion.

Thiazides are contraindicated because they increase the blood levels of uric acid.

Urine Alkalinization

Urine alkalinization favors the conversion of the uric acid to urate and decreases tubular crystals precipitation.

However, alkalinization decreases calcium phosphate solubility and favors crystals precipitation in renal tubules and soft tissues as well as alkalosis increases the amount of calcium that is bound to albumin and favors arrhythmia and tetany.

Therefore, urine alkalinization is not recommended as it may even be dangerous.

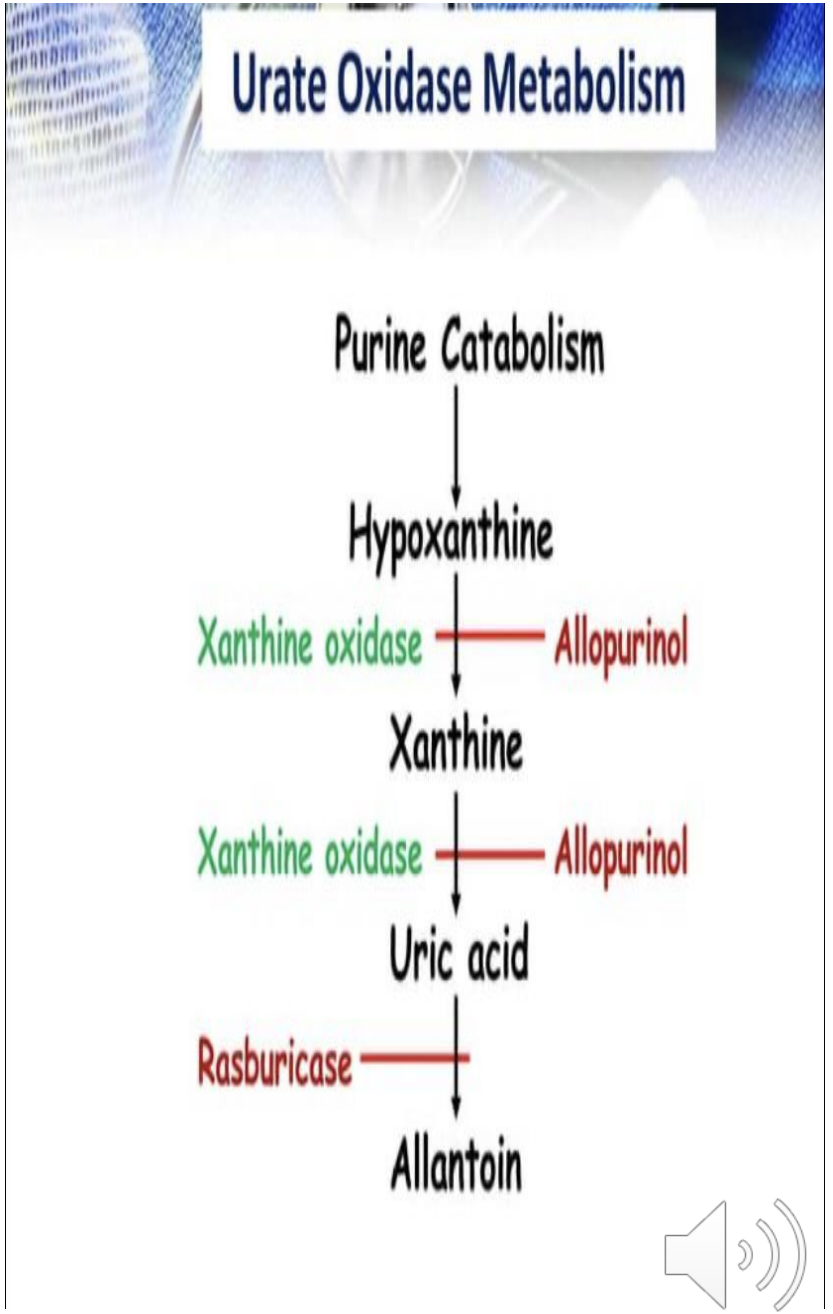
Allopurinol

- Allopurinol is a purine analogue and is the isomer of hypoxanthine.
- It is metabolized by xanthine oxidase to oxypurinol (the active form of allopurinol), which is a competitive inhibitor of xanthine oxidase.
- This leads to a weak response to treatment in patients with TLS and severe hyperuricemia as well as serum concentration of hypoxanthine and xanthine increases after allopurinol and xanthine can precipitate into the renal tubules, leading to AKI.

- **it is recommended to use allopurinol as a prophylactic treatment and not in established TLS, where it can be used only if the patient is allergic to rasburicase or has glucose-6-phosphate dehydrogenase (G6PD) deficiency.**

- Doses:
- for adults: 200–400 mg/m^2/day, divided in 1 to 3 doses, to maximum 800 mg/day;
- for children: 300–450 mg/m^2/day in 3 doses, to maximum 400 mg/day
- In chronic kidney disease, the dose is adjusted according to estimated glomerular filtration ratio (eGFR)

- **Prophylactic therapy must begin at least 24 h prior to chemotherapy initiation and must be continued for at least 7 days.**



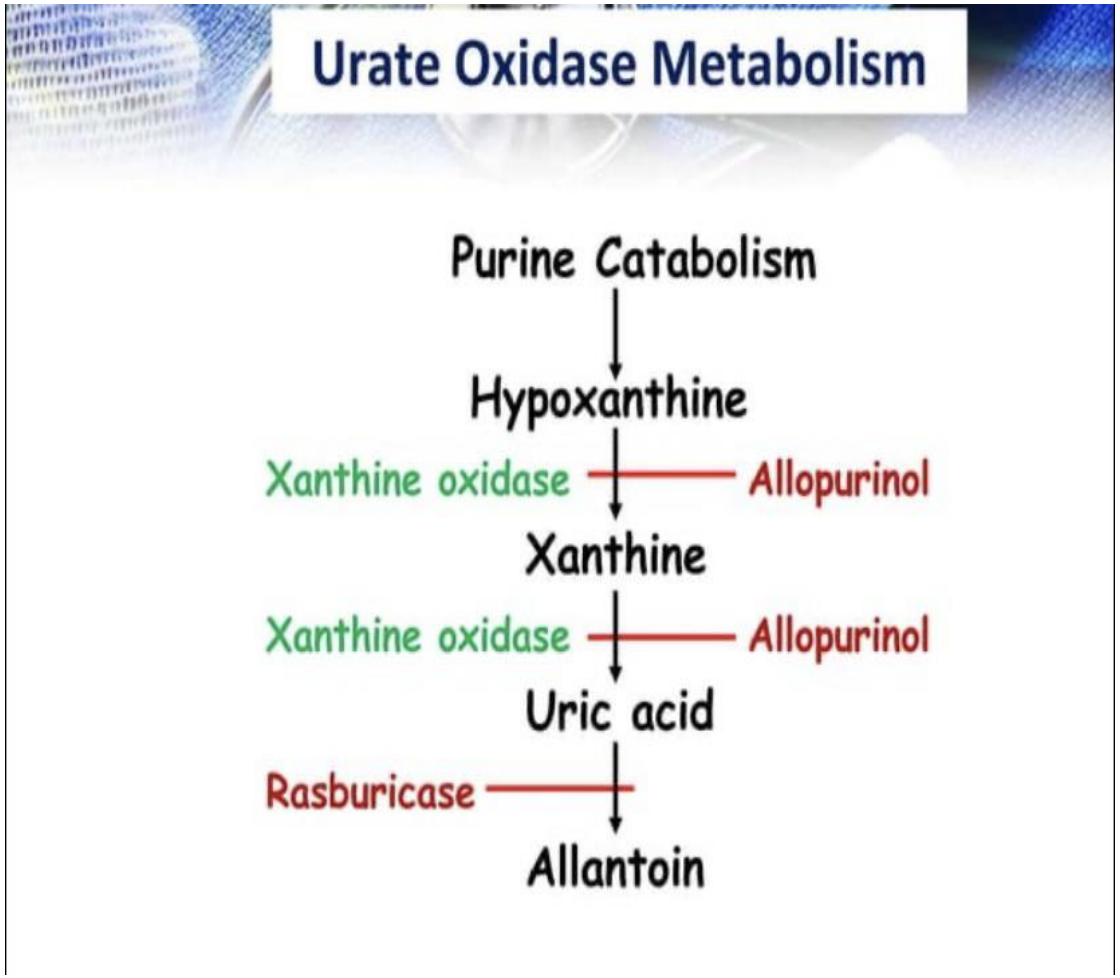
Allopurinol

- Allopurinol has multiple drug interactions;
- It is recommended to lower the doses for 6-mercaptopurine and azathioprine with 65–75% when these drugs are administered together with allopurinol.
- Moreover, other drugs for which doses should be adjusted in this situation are thiazides, cyclophosphamide, cyclosporine, ampicillin, and amoxicillin.

- **Side effects are rare but may be life-threatening:**
- Steven–Johnson syndrome up to toxic epidermal necrolysis, acute toxic hepatitis, small vessel vasculitis, bone marrow aplasia, and DRESS syndrome (eosinophilia, rash, fever, lymphadenopathy, acute hepatitis, acute interstitial nephritis

Febuxostat

- Febuxostat is a new inhibitor of xanthine oxidase.
- It does not induce the hypersensitivity reactions seen with allopurinol and it does not necessitate dose adjustment according to eGFR, so it is an alternative to allopurinol in certain groups of patients.
- A recent meta-analysis included six studies and was performed in order to evaluate the efficacy and safety of febuxostat compared to allopurinol as a prophylaxis for TLS; more than half of all the patients from this **meta-analysis came from the FLORENCE trial.**
- **Both drugs showed a similar TLS incidence** (OR 1.01, 95%CI: 0.56–1.81) and response rate (OR 1.01, 95%CI: 0.55–3.51)



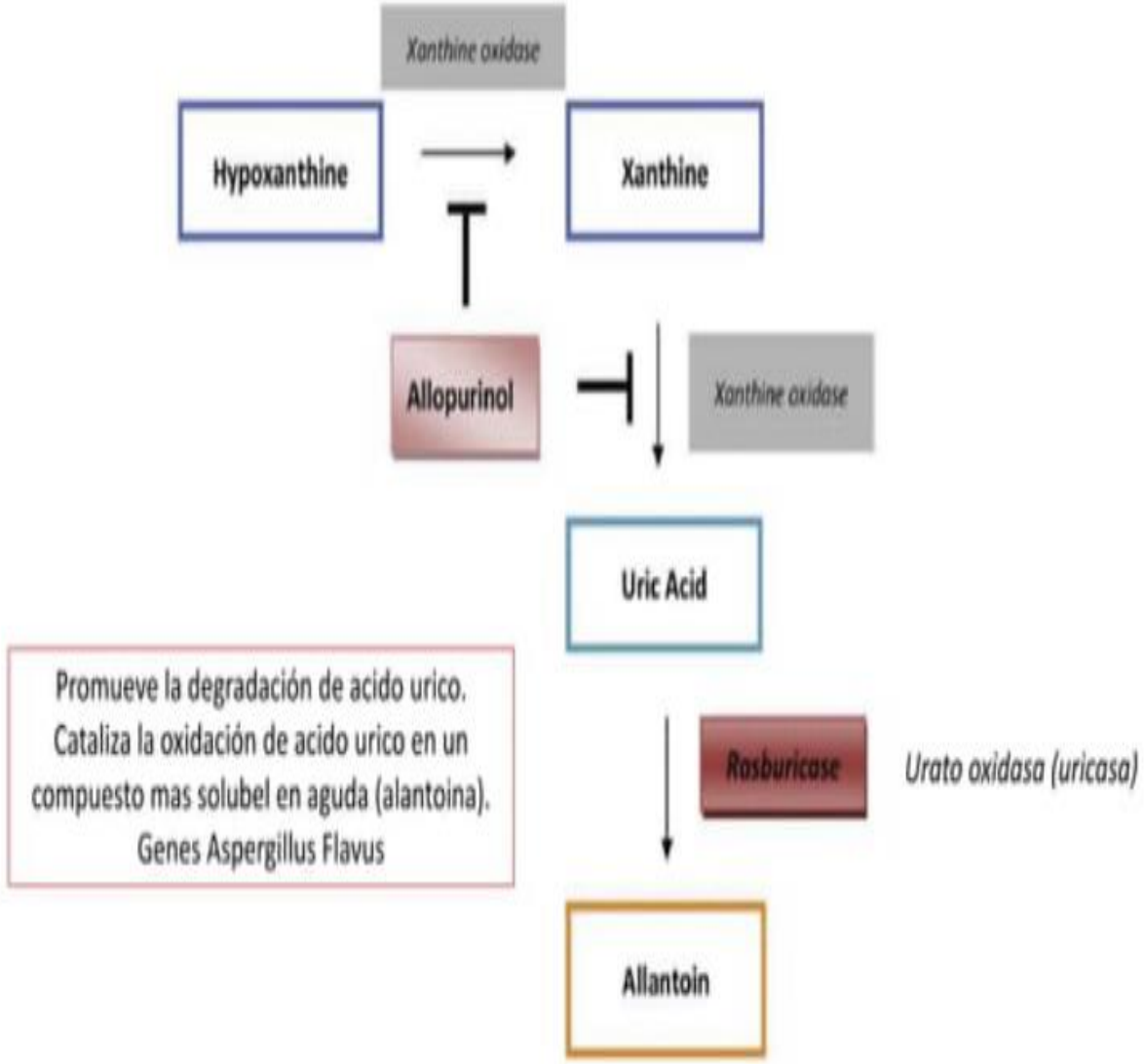
Rasburicase is a recombinant variant of UO, derived from Aspergillus flavus.

It converts uric acid in allantoin, carbon dioxide and hydrogen peroxide.
Accumulation of hydrogen peroxide in patients with G6PD deficiency leads to methemoglobin accumulation leading to hemolytic anemia

Rasburicase can be used for TLS prevention in high-risk patients and for the treatment of already-constituted TLS.

It is recommended as a prophylaxis to high-risk patients in a single dose of 3 mg to adults and 0.2 mg/kg to children.
It can be repeated daily for 5–7 days when necessary (lack of response or increase in the uric acid level)

RASBURICASA



Dubbs et al Rapid Fire: Tumor Lysis Syndrome Emerg Med Clin N Am 2018

Allopurinol vs Rasburicase

- In a multicenter trial, 52 pediatric patients with hematologic malignancy at high risk for TLS were randomly assigned to receive allopurinol or rasburicase.
- Uric acid levels

Rasburicase	Allopurinol
Dec by 85%	Dec by 12%

- Pui and colleagues administered rasburicase IV at doses up to 0.2 mg/kg in 131 pediatric patients with newly diagnosed leukemia or lymphoma.

Initial uric acid	4 hours	24 hours
9.7 mg/dl	1mg/dl	0.5 mg/dl

The study showed a better response for the patients treated exclusively with rasburicase.
The uric acid was reduced in 87% of cases treated with rasburicase, versus 78% cases treated with rasburicase followed by allopurinol, versus 66% of cases treated with allopurinol

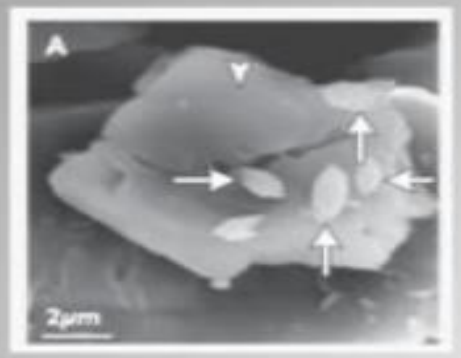
Treatment

- TLS necessitates a multidisciplinary approach and a careful monitoring of some key elements:
- It is recommended to maintain a urine output of at least 100 mL/m^2/h for adults and 4 mL/kg/h for children.
- Urine alkalinization is not recommended
- It is recommended to administer **rasburicase and not xanthine oxidase inhibitors**.

- The only indications for xanthine oxidase inhibitors are known rasburicase allergy and G6PD deficiency
- The recommended dose of rasburicase is 0.2 mg/kg/day, and the treatment duration must be established according to clinical response, but no more than 3 to 7 days

- Some studies still recommend a fixed, single dose of 6 mg, which was found to be as effective as the weight-adapted dose

Biomedicines **2022**, *10*(5), 1012; https://doi.org/10.3390/biomedicines10051012



Hyperuricemia

Uric Acid
Low <4
Intermediate: 4-8
High >8

Flush out uric acid

- NS 2500-3000mL/m²/day
- Goal: UO – 80-100mL/m²/hr

Metabolize Uric Acid

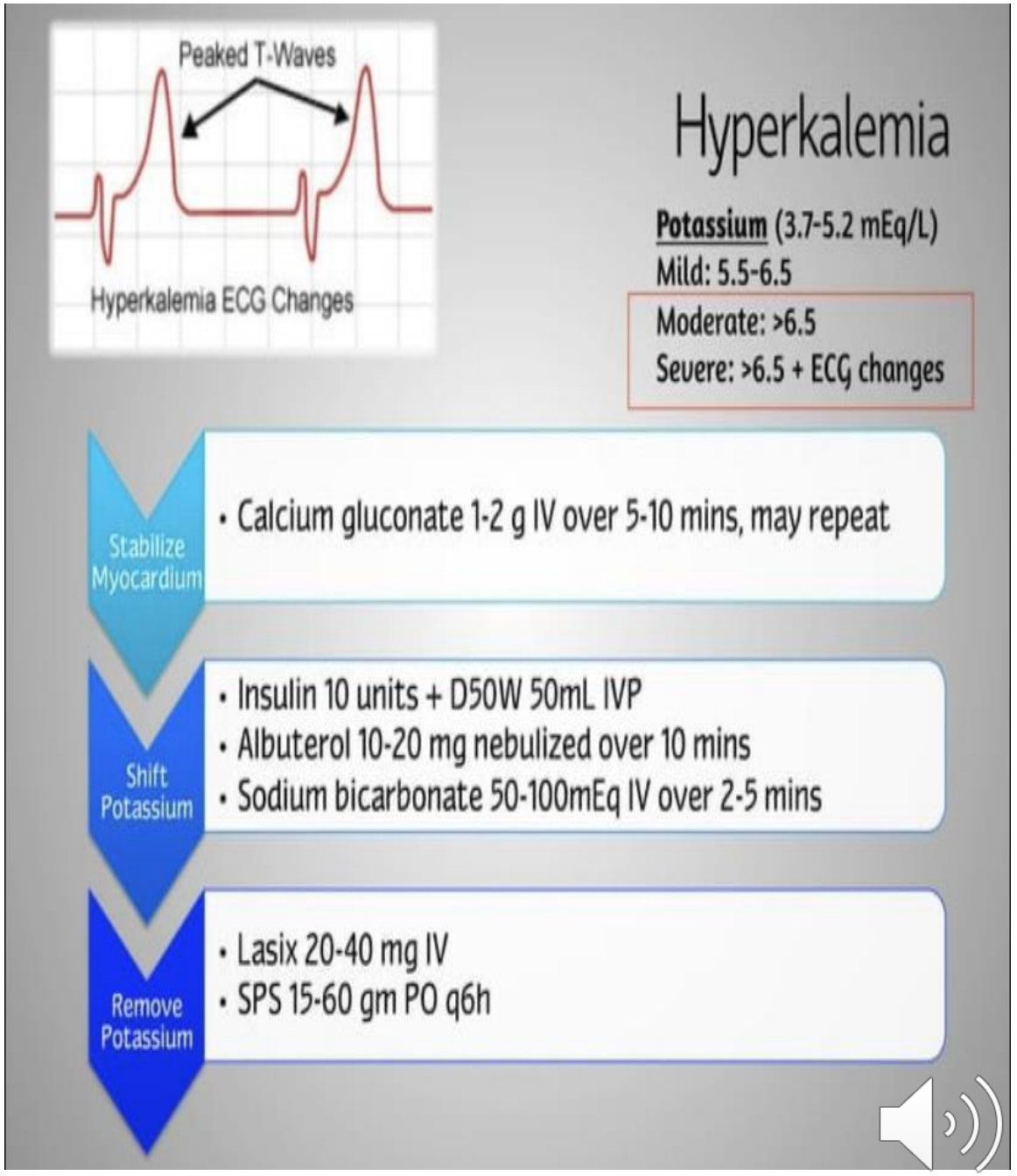
- Rasburicase 0.2 mg/kg IV x 1, redose based upon UA levels

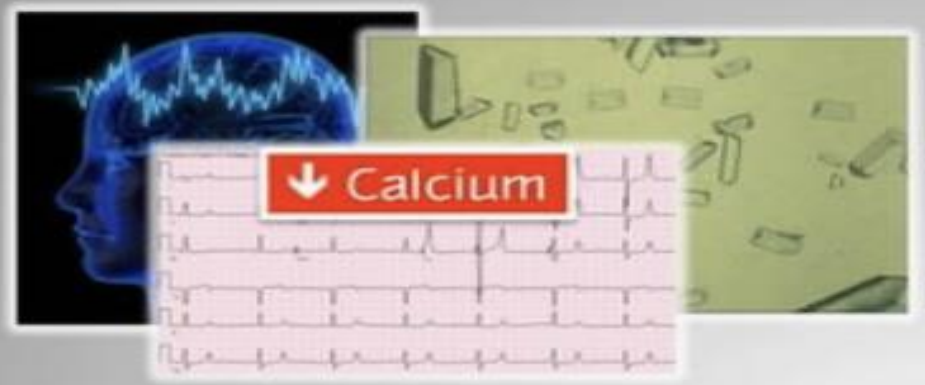
• Calcium Supplementation

- **Calcium is not routinely recommended**, because it increases the precipitation of calcium in the soft tissues and it aggravates AKI.
- Calcium administration is recommended : severe and symptomatic hypocalcemia (tetany, Chvostek sign, muscular fasciculation, bronchospasm, laryngospasm, seizures), changes of the electrocardiogram, and arrhythmia.

• Treating Hyperkalemia

- When potassium value increases with more than 25% compared to baseline value or when kalemia reaches 6 mmol/L, cardiac monitoring is recommended, altogether with the standard treatment:
- beta-adrenergic agonists (albuterol), glucose-insulin solution, short calcium gluconate infusion for myocardial protection, loop diuretics, and potassium binding resins in order to increase digestive loss.
- When **kalemia exceeds 7 mmol/L, dialysis** is recommended.





Hyperphosphatemia

Phosphate (2.4-4.1 mg/dL)
Ca x Phos > 70

Phosphate Binders (prevent absorption via GI tract)

↓Renal fxn	Aluminum Hydroxide 300 mg PO with meals
↑Ca	Calcium Acetate 1337 mg PO TID AC
	Sevelamer 800-1600mg PO TID AC

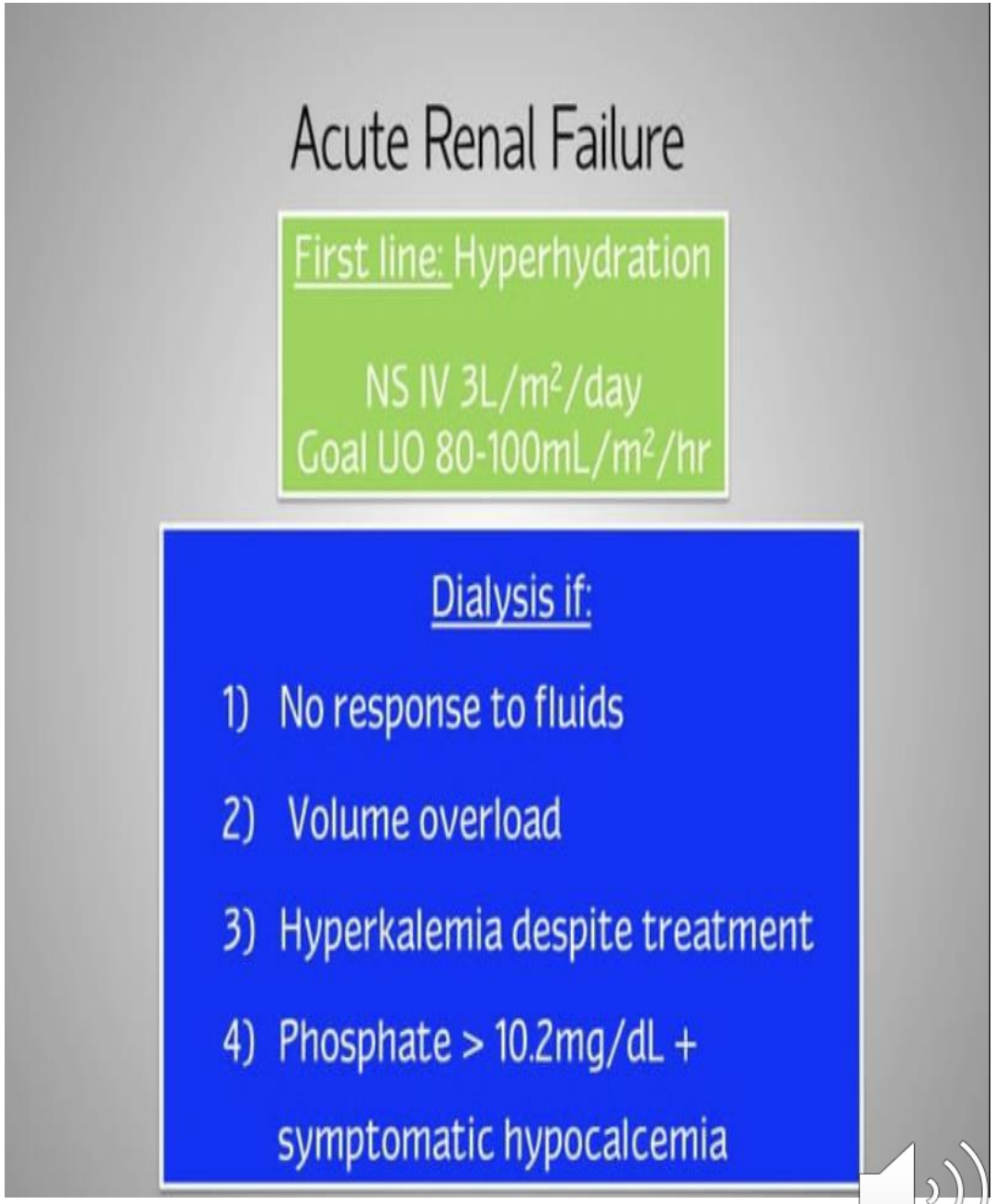
Renal Replacement Therapy

- RRT is indicated ,when the patient develops hypervolemia, or when electrolyte disturbances are refractory to medical treatment.

- The options for RRT are:

- daily hemodialysis;
- continuous veno-venous hemofiltration;
- Combination of intermittent hemodialysis and continuous hemofiltration/hemodiafiltration for an efficient clearance of phosphate, which is time dependent.

- Peritoneal dialysis is not adequate, because it offers a less efficient clearance of uric acid and phosphate.
- patients may associate abdominal complications related to neoplasia (peritoneal carcinomatosis, compartment syndrome), which are contraindications for this procedure.



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Future Perspectives

Prevention through Chemotherapy Modulation

- The risk of TLS can be diminished through choosing less aggressive chemotherapy, allowing enough time for the compensatory kidney mechanisms to remove the products derived from tumor lysis.

- The Berlin–Frankfurt–Muenster group treated a child with ALL by initially administering prednisone for one week before initiating induction chemotherapy .

- **Other Options for Enzyme Replacement Therapy**

- **Oral recombinant urate oxidase (ALLN-346),**
- It targets intestinal degradation of urate, was studied in mice deficient in uricase with severe hyperuricemia
- **Pegloticase** is a recombinant porcine uricase that is pegylated to increase its elimination half-life and to decrease the immunogenicity.
- It treatment of severe, refractory gout.
- It is given as an intravenous infusion every two weeks
- Like rasburicase, it is contraindicated in patients with G6PD deficiency.


Thank
you !