# Hematological Malignancies and the Palliative Care Provider – What **is** the Goal of Care?

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# Outline

- Cases
- Background – heme malignancy + palliative care
- Top 3 Pearls
  - Unique side effects of treatment
  - Importance of transfusion support
  - Uncertainty about the goals of care
- Questions – What perplexes you about heme malignancies?

# Cases

- 21 yo woman with B-ALL that relapsed 1 year after an allogeneic stem cell transplant.

While undergoing treatment on an investigational CAR-T trial, she experiences high fevers, abnormal liver function tests, profound cytopenias and hypotension.

*What is happening to her and what is the goal of this CAR-T treatment?*

# Cases

- 55 yo woman five years out from an allogeneic stem cell transplant for blast phase CML.  Post transplant she had early relapse but achieved a remission with rapid withdrawal of immunosuppression, DLI, and re-initiation of TKI.  She has no evidence of leukemia but lives with moderate chronic GVHD of the eyes, skin, and vagina.

*Would we have expected her to be cured?  How can we best help her now?*

# Cases

83 yo woman with a history of breast cancer and therapy-related AML has been treated with hypomethylating agent + venetoclax for over a year.  She is in remission but experiences fatigue from this therapy and dislikes the frequent visits and labs.

*Is she cured? Can she stop treatment?  How can we best support her?*

# Cases

40 yo man with high risk AML.

- Needed multiple cycles of chemotherapy to achieve a remission
- Underwent a curative-intent allogeneic SCT
- Has relapse on D+45

Undergoing chemotherapy

*What is the purpose of this therapy?*

# Background

- Symptom burden HIGH
  - Lack of energy, fatigue, poor sleep, dry mouth, pain
- Intensive treatments with prolonged hospital stays
- High psychological distress
  - Depression + anxiety in 30-60% of patients
  - Acute stress reactions + PTSD
- Lack of information – prognostic uncertainty, misperceptions in treatment goal/risks
- Toll of "indolent" diseases
- Cure at a cost

El-Jawahri et al.

# Top 3 Pearls

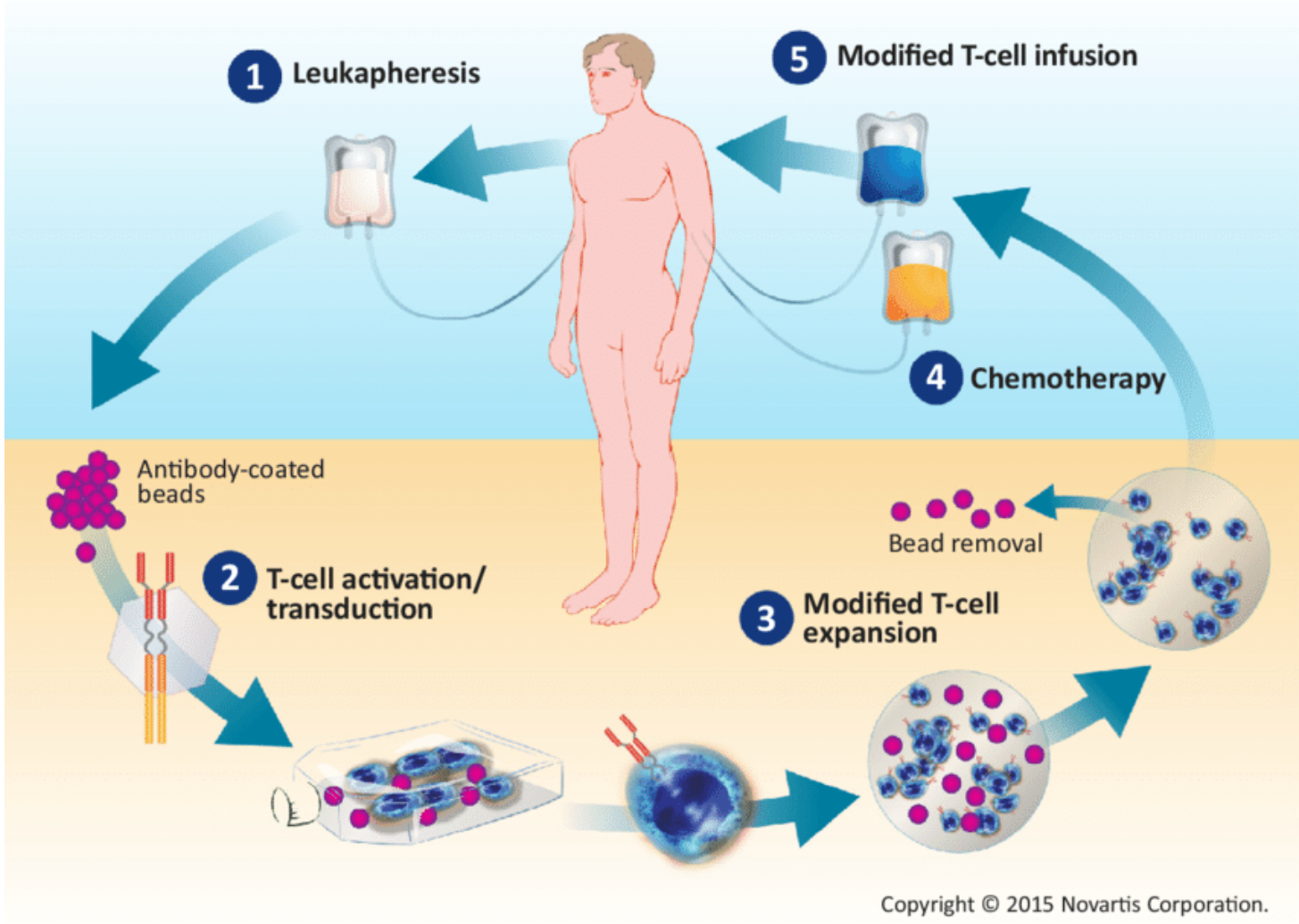
3. **Unique side effects**
2. Importance of blood transfusions
1. Challenge to define goal of care with prognostic uncertainty high

# Unique Side Effects

- CAR-T/Bi-Specific T cell engagers
  - CRS
  - ICANs
  - HLH like phenomenon
- Allo HSCT
  - GVHD – acute + chronic

# CAR-T

- Chimeric Antigen Receptor T-cells
- Used to treat:  lymphoma, leukemia (CLL, ALL), myeloma
- Curative??



# CAR-T

- Side effects:
- *Cytopenias, toxicity from the chemotherapy*
- Cytokine release syndrome (CRS)
- Neurological toxicity – aka ICANS (immune effector cell-associated neurotoxicity syndrome)
- HLH like phenomenon

# CRS

- **Fever**, rigors
- Malaise
- Anorexia
- **Hypotension**
- **Hypoxia**
- Any organ dysfunction

| Parameter | Grade 1 | Grade 2 | Grade 3 | Grade 4 |
|---|---|---|---|---|
| *Fever* | T >38 | T>38 | T>38 | T>38 |
| *Hypotension* | None | No pressors | Pressors | Multiple pressors including vasopressin |
| *Hypoxia* | None | O2 by low flow NC | O2 by HFNC, facemask, NRB, VM | Positive pressure ventilatory support |

ASTCT Grading Criteria -- CRS

# ICANS

- Toxic encephalopathy
- Word finding difficulty
- Confusion
- Dysphasia/aphasia
- Impaired fine motor skills
- Somnolence
- Seizures
- Motor weakness
- Cerebral edema
- coma

**Immune-effector cell-associated encephalopathy tool (ICE)**

- Orientation: year/month/city/hospital 4 points
- Naming: 3 objects, 3 points
- Following commands: 1 point
- Writing: 1 point
- Attention: Count backwards from 100 by 10, 1 point

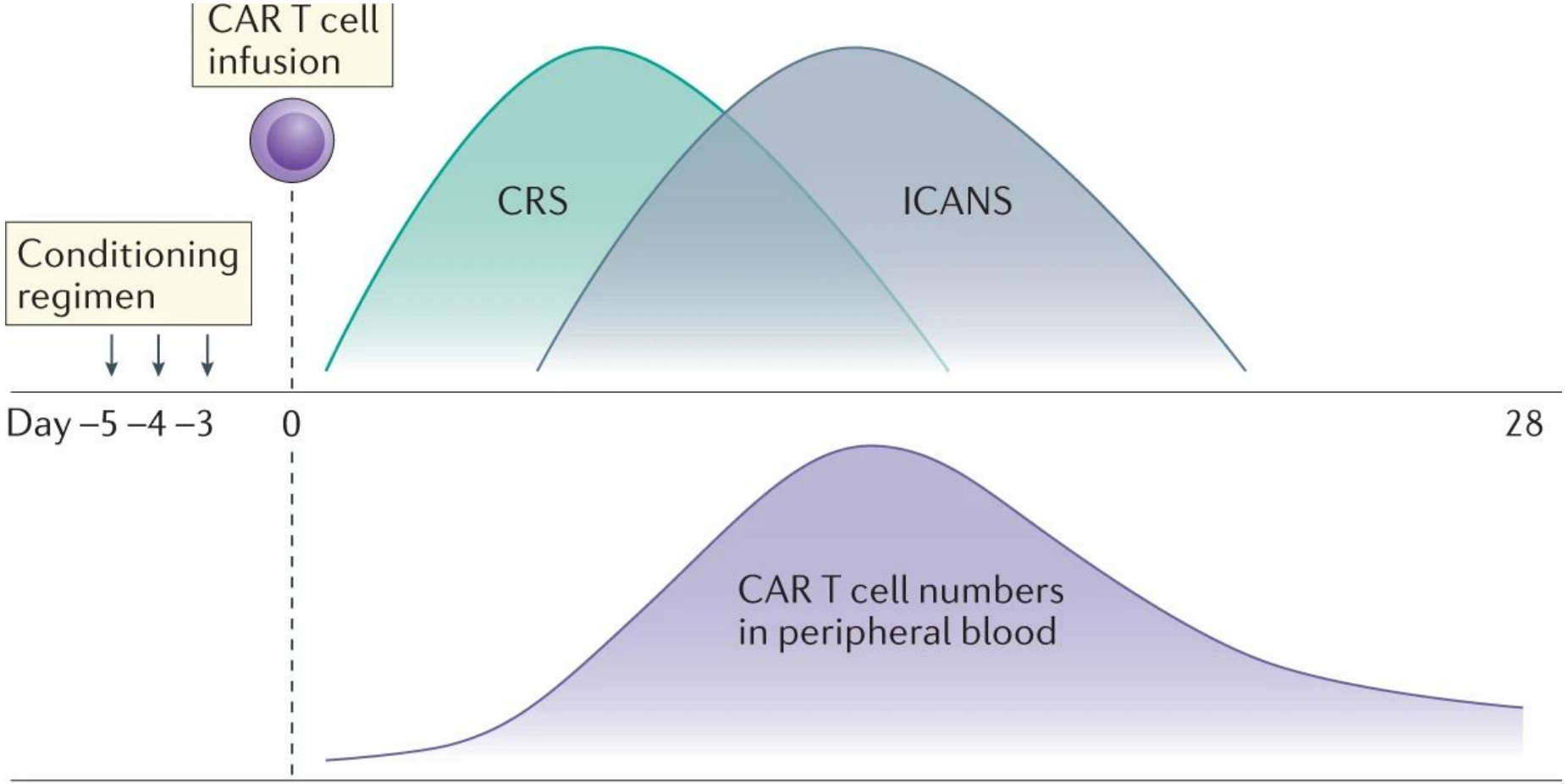
**Total: 10 points**

| Parameter | Grade 1 | Grade 2 | Grade 3 | Grade 4 |
|---|---|---|---|---|
| ICE score | 7-9 | 3-6 | 0-2 | 0 |
| Level of consciousness | Awakens spontaneously | To voice | To tactile stimuli | To vigorous tactile OR unarousable, stupor or coma |
| Seizure | NA | NA | Any minor seizure | Any major seizure |
| Motor findings | NA | NA | NA | Significant focal motor weakness |
| Increased ICP/edema | NA | NA | Focal edema | Diffuse edema, posturing |

ASTCT Grading Criteria -- neurotox

**Treatment:**

1. Tocilizumab
2. Dexamethasone
3. IT corticosteroids +/- chemo
4. Anakinra
5. Rehab?




Morris et al

# HLH

- Clinical syndrome of pathological hyperinflammation and uncontrolled macrophage activation
- Previously seen in auto-immune conditions or with viral triggers
- Now seeing as a “severe” manifestation of CRS after CAR-T therapy

# CRS/ICANS

- Frequency/severity/timing -- VARY
- Also seen with other drugs… (blinatumomab, teclistimab, etc) due to similar MOA of CAR-T
- Similar type of technology is being used more frequently to treat solid tumor malignancies – would expect similar toxicity

# Cases

- 21 yo woman with B-ALL that relapsed 1 year after an allogeneic stem cell transplant.

While undergoing treatment on an investigational CAR-T trial, she experiences high fevers, abnormal liver function tests, profound cytopenias and hypotension.

*What is happening to her and what is the goal of this CAR-T treatment?*

*HLH – severe manifestation*

*Cure?*

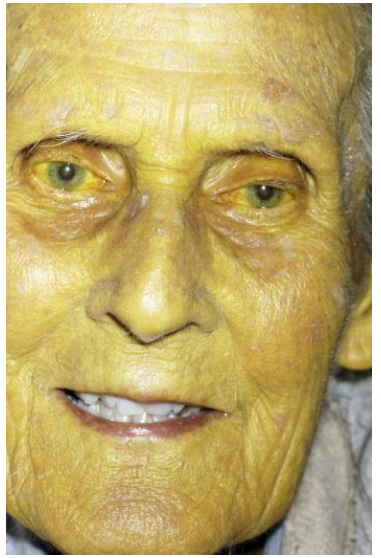
# Allogeneic SCT

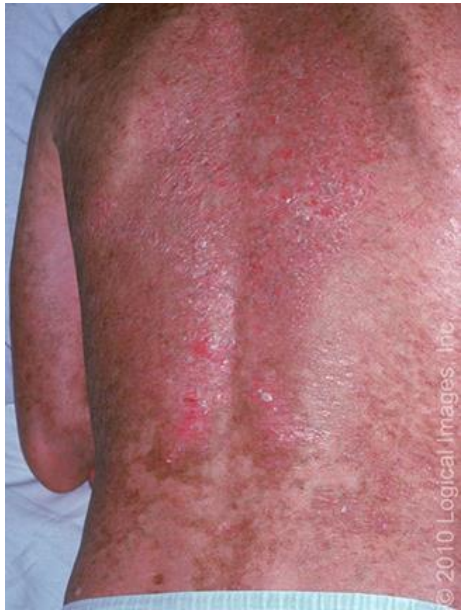
- Tool to replace a malfunctioning or cancerous bone marrow with a donor's stem cells
- Entails variable doses of chemotherapy prior to the transplant
- Prolonged hospital stay with initial side effects similar to cytotoxic chemotherapy
- Used for acute leukemias, myelodysplastic syndrome, lymphomas, bone marrow failure states

Goal=Cure

Relapse = Possible

# Allogeneic SCT -- GVHD






Graft-Versus-Host Disease

**Acute**:

- <D100
- Only 3 organs
  - Skin
  - Gut
  - Liver
- 40-70% of all SCT recipients
- Gets better, or doesn't

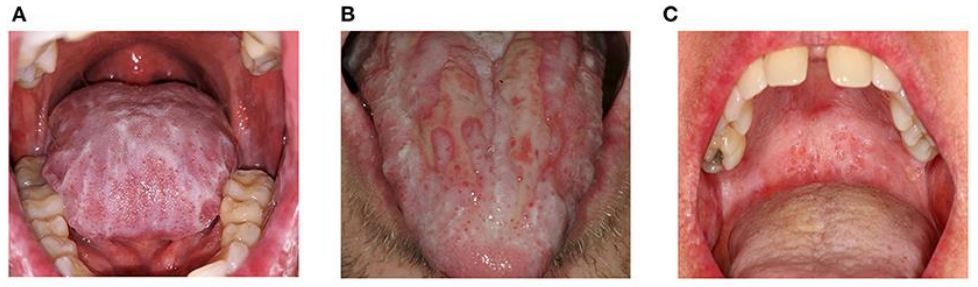
*Treatment:*

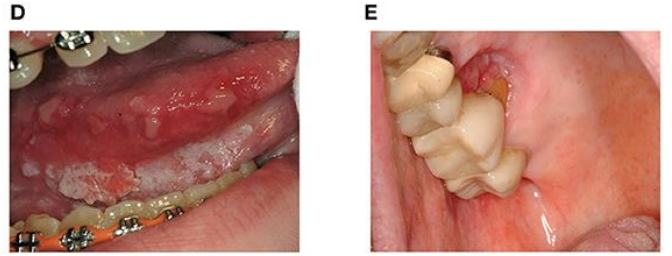
- Prevention
- Steroids—all forms – high dose →AEs
- Other immunosuppressive meds – ruxolitinib, MMF, tacrolimus, ATG, alemtuzumab, pentostatin, infliximab→AEs
- ECP
- Clinical trials

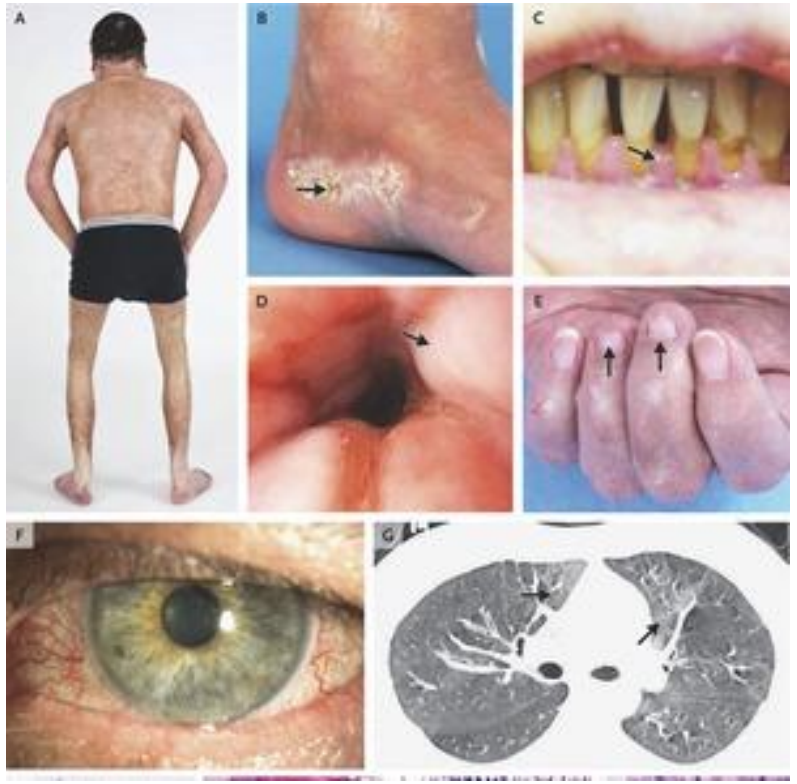
# Allogeneic SCT -- GVHD

**Chronic GVHD**

- >D100
- Protean manifestations
  - Skin
  - Oral
  - Ocular
  - MSK
  - Lungs
  - GU
- Treatment aimed at CONTROL, often hard to eradicate



# Allogeneic SCT -- GVHD

**Treatment:**

- Topical steroids
- Systemic steroids -- ~1 mg/kg/day -- slower taper
- Immunosuppressant medications:  CNIs/MTORi, Ruxolitinib, ibrutinib, imatinib, rituximab
- ECP
- Belmosudil – ROCK inhibitor

It takes a village!

-ophthalmology – scleral lenses, auto eye gtt

-dermatology

-pulmonology

-OB-GYN

-psychology/psychiatry

# Cases

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*Would we have expected her to be cured?  How can we best help her now?*

Example of how hard prognostication is!

Great OB-GYN, ophthalmologist, health psychologist

# Top 3 Pearls

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2. **Importance of blood transfusions**
1. Challenge to define goal of care with prognostic uncertainty high

# Blood Transfusions

- RBC+platelet transfusions are critical early in care of heme malignancy patients
  - 50-90% of MDS patients need a RBC transfusion, many become dependent[1]
  - ~9 units of blood, 7 units of platelets during induction[2]
- Upon transitioning to a non-curative setting, asking patients + physicians to forego these transfusions is a barrier – “transfusion tether”


1. Wood et al
2. Liron Miller et al

# Cases

83 yo woman with a history of breast cancer and therapy-related AML has been treated with hypomethylating agent + venetoclax for over a year. She is in remission but experiences fatigue from this therapy and dislikes the frequent visits and labs.

*Is she cured? Can she stop treatment? How can we best support her?*

This is NON-CURATIVE therapy. It is likely her AML will recur w/o this therapy and yet with this therapy, she needs close monitoring of labs and intermittent transfusions. She would likely benefit from dual management of palliative care and hematology.

# Top 3 Pearls

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**1. Challenge to define goal of care with prognostic uncertainty high**

# Heme Malignancies + Palliative Care Services

- More chemo at EOL
- More ER visits/hospital admits/ICU stays/significant time in the hospital near EOL
- Much more likely to die within 3 days of enrollment on Hospice compared to solid tumor patients

WHY?

1. Blood transfusions
2. **Lack of clarity in GOC -- *prognostic uncertainty***

Le Blanc et al.

# Cases

40 yo man with high risk AML.

- Needed multiple cycles of chemotherapy to achieve a remission
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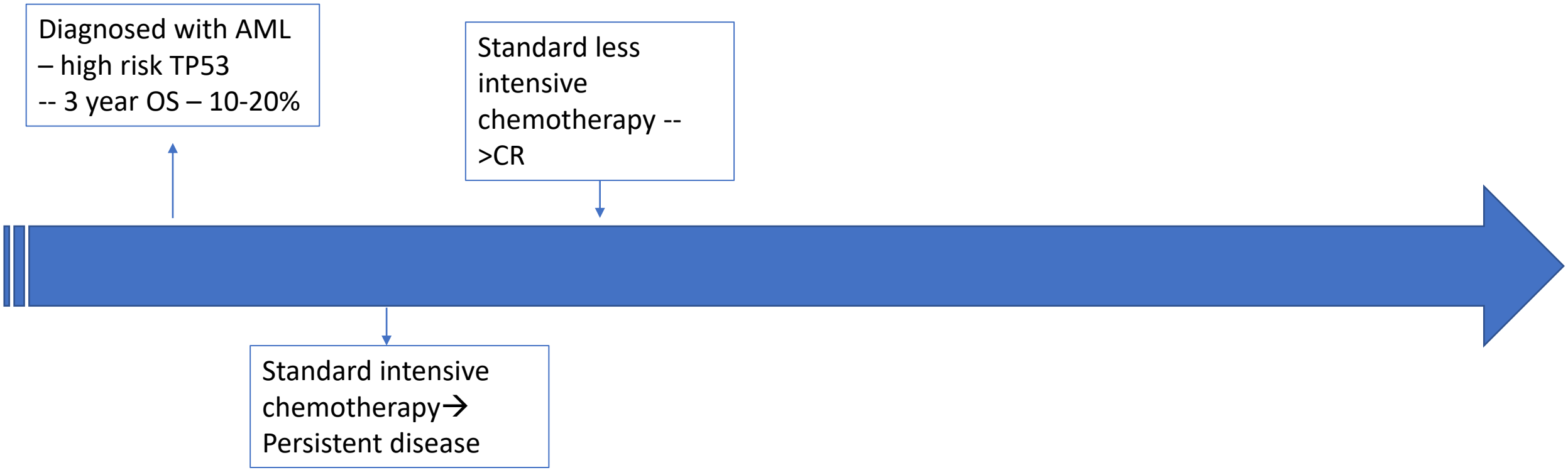
- Has relapse on D+45

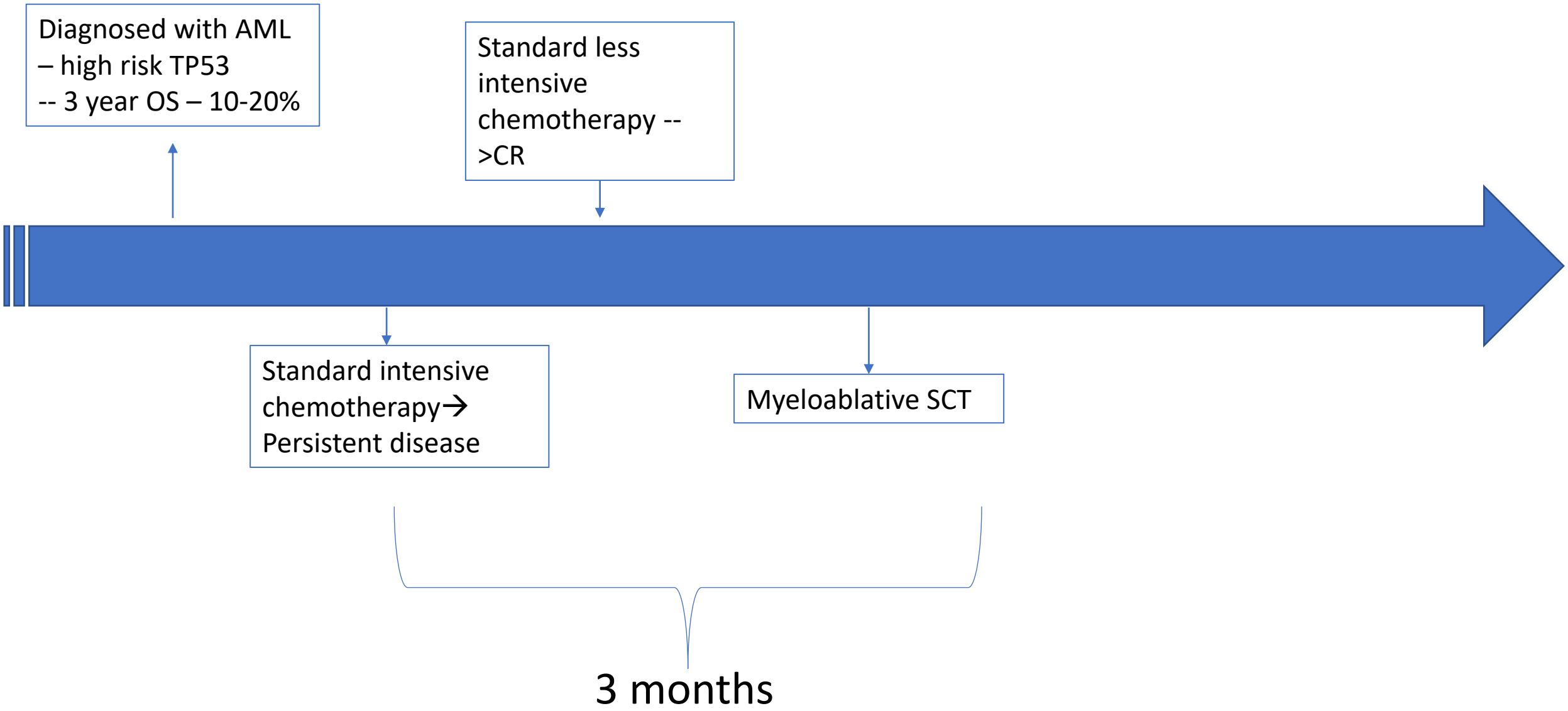
Undergoing chemotherapy

*What is the purpose of this therapy? When is the right time for palliative care?*


Diagnosed with AML
– high risk TP53
-- 3 year OS – 10-20%


Diagnosed with AML
– high risk TP53
-- 3 year OS – 10-20%
Standard intensive chemotherapy→
Persistent disease


Diagnosed with AML
– high risk TP53
-- 3 year OS – 10-20%
Standard less intensive chemotherapy -- >CR
Standard intensive chemotherapy→ Persistent disease


Diagnosed with AML
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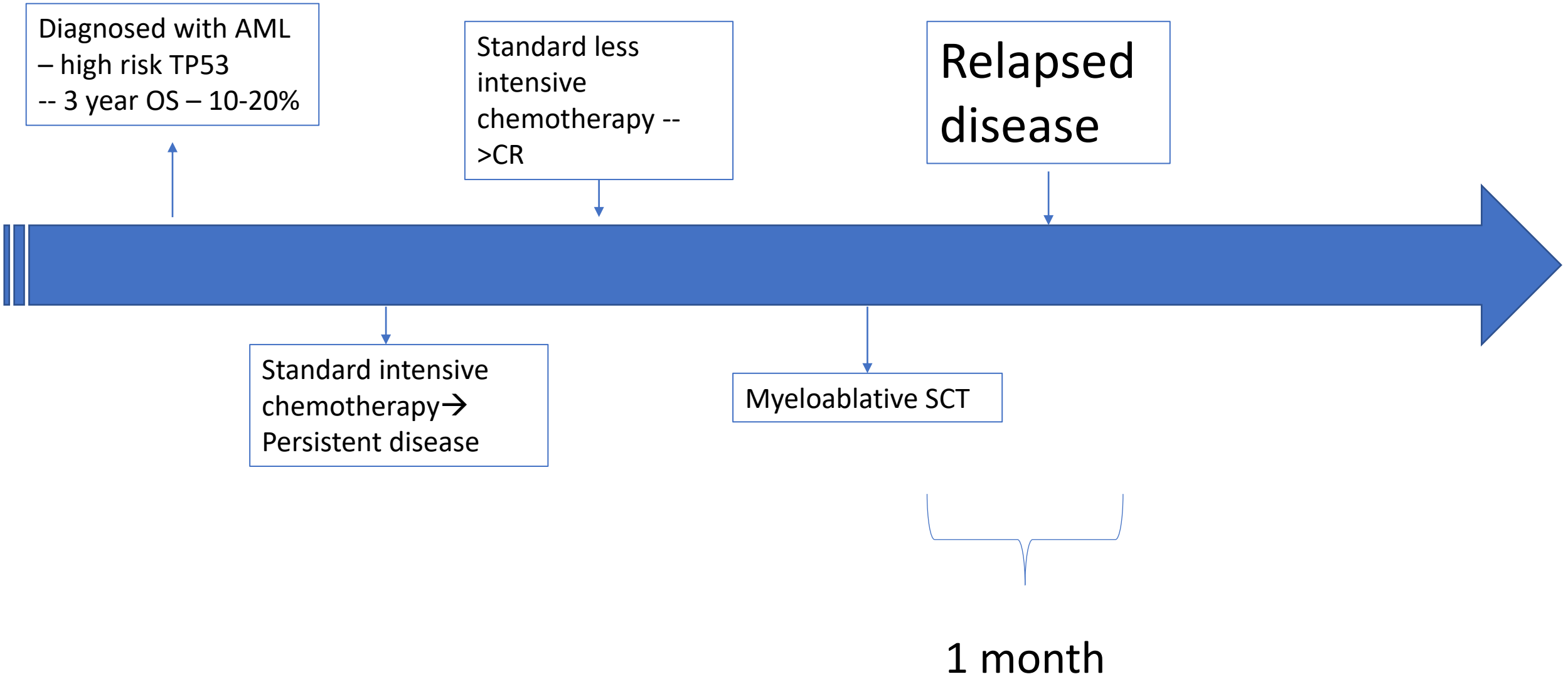
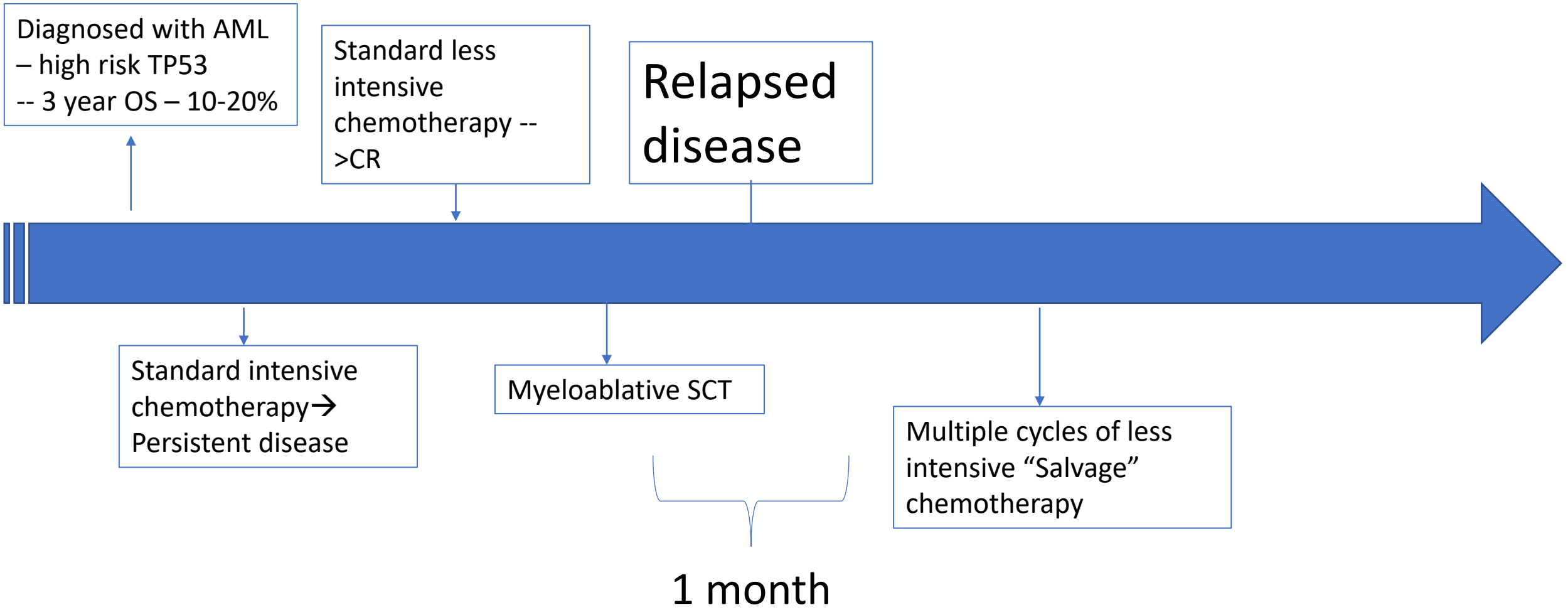
-- 3 year OS – 10-20%
Standard less intensive chemotherapy --
>CR
Standard intensive chemotherapy→
Persistent disease
Myeloablative SCT
3 months


Diagnosed with AML
– high risk TP53
-- 3 year OS – 10-20%
Standard less intensive chemotherapy -- >CR
Relapsed disease
Standard intensive chemotherapy→ Persistent disease
Myeloablative SCT
1 month


Diagnosed with AML
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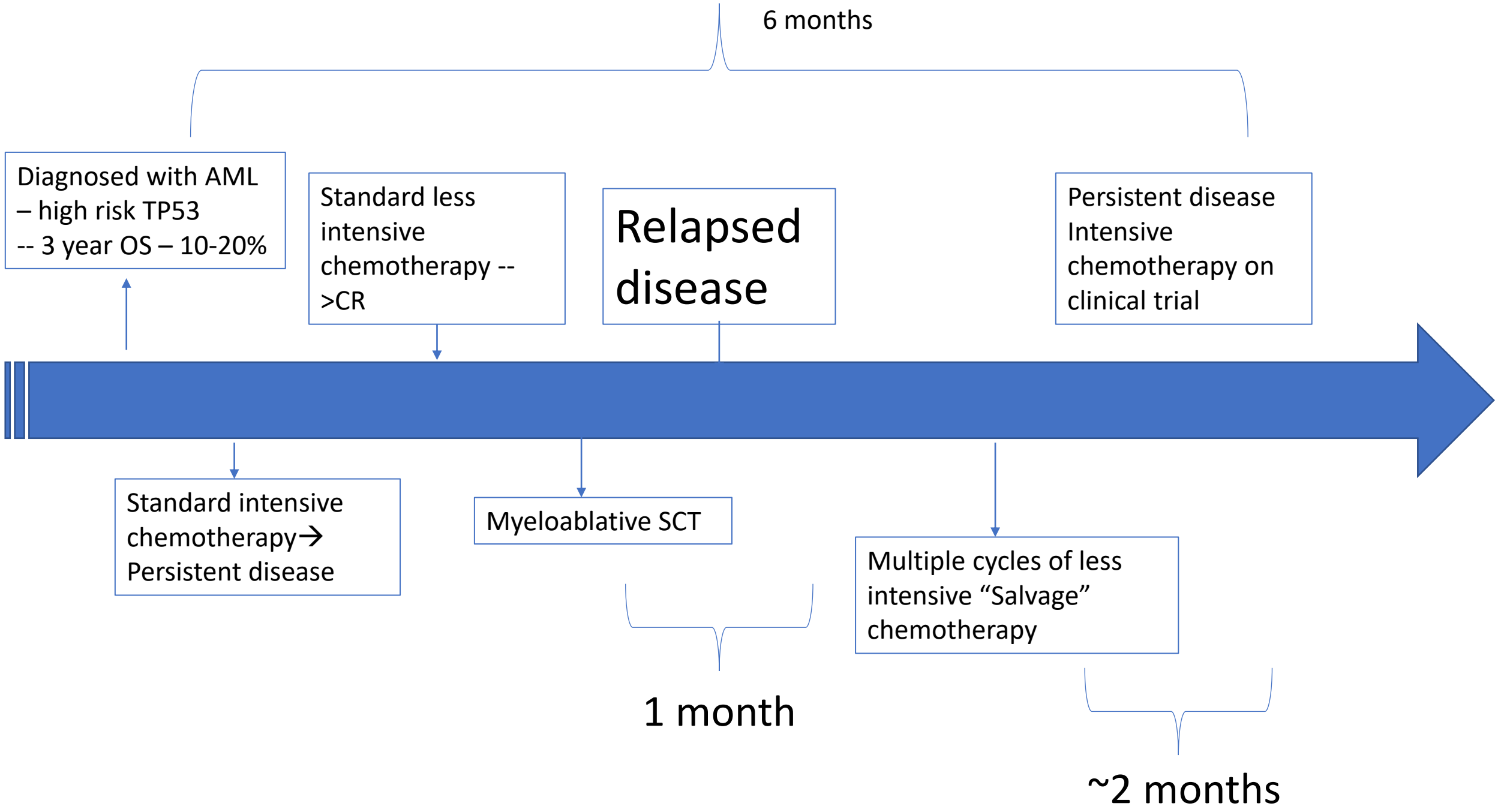
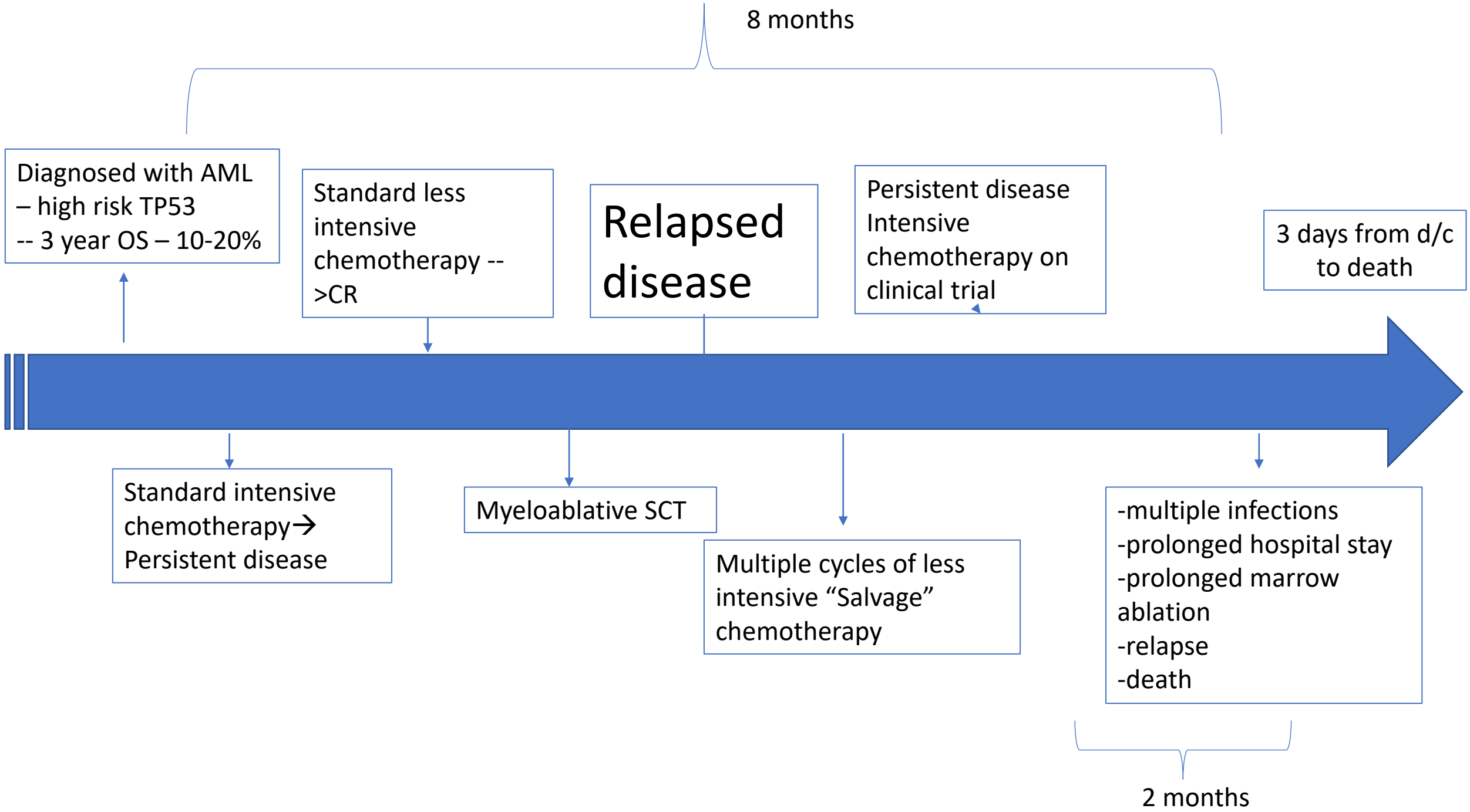
Standard less intensive chemotherapy -- >CR
Relapsed disease
Standard intensive chemotherapy→ Persistent disease
Myeloablative SCT
Multiple cycles of less intensive “Salvage” chemotherapy
1 month


6 months
Diagnosed with AML – high risk TP53 -- 3 year OS – 10-20%
Standard less intensive chemotherapy -- >CR
Relapsed disease
Persistent disease Intensive chemotherapy on clinical trial
Standard intensive chemotherapy→ Persistent disease
Myeloablative SCT
Multiple cycles of less intensive “Salvage” chemotherapy
1 month
~2 months


8 months
Diagnosed with AML – high risk TP53 -- 3 year OS – 10-20%
Standard less intensive chemotherapy -- >CR
Relapsed disease
Persistent disease Intensive chemotherapy on clinical trial
3 days from d/c to death
Standard intensive chemotherapy→ Persistent disease
Myeloablative SCT
Multiple cycles of less intensive “Salvage” chemotherapy
-multiple infections
-prolonged hospital stay
-prolonged marrow ablation
-relapse
-death
2 months

# Questions?

# References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