ANZTCT CONSENSUS PRACTICE STATEMENT

Optimising Allogeneic HSCT in Acute Myeloid Leukaemia

Ashish Bajel, Genevieve Douglas, Karen McCleary, Vajiranee Malalasekera, Gaurav Sutrave, Julian Cooney, Edward Abadir, Devendra Hiwase, Hock Choong Lai, Richard Doocey, Shaun Fleming, Ashley McEwan, Caroline McNamara, Nada Hamad

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Disclosures

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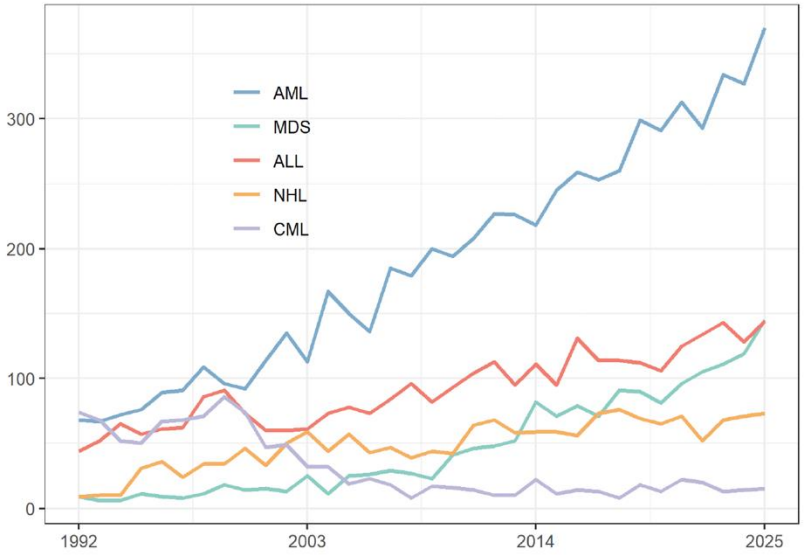
Outline

- Why - case for a pre-transplant AML guidance framework in Australia and New Zealand
- How
- What - the practice recommendations
- Next steps and future opportunities

Why – The clinical stakes in AML

Allogeneic HSCT

Curative Modality



1 **Rapid therapeutic change**

Genomic profiling, MRD assessment, and targeted/low-intensity agents have transformed risk stratification and achievement of remission

2 **High response, but relapse persists**

Novel drugs (VEN–AZA, FLT3 and menin inhibitors, CPX-351) lift remission rates, yet relapse remains common.

3 **Increasing need for transplant**

More patients now reach remission and become transplant-eligible — sharpening the need for clear referral pathways.

A critical — and locally complicated — window

The pre-transplant period matters

Treatment choices made before transplant directly shape whether allo-HSCT remains feasible .

Diagnostics, and response tools must be actively adapted to protect — not delay — transplant eligibility.

Local realities in Australia & New Zealand

- ✓ Unequal access to novel agents across centres
- ✓ Different funding & reimbursement pathways (PBS/TGA vs Medsafe/Pharmac)
- ✓ Geographic disparities in specialist and transplant services
- ✓ Logistical challenges coordinating transplant amid rising demand

Complement not replace

- Intended alongside ELN 2022, ELN 2024, ELN MRD 2025, NCCN, AML Optimal Pathway and National AML treatment guidelines
- Focus on AML–transplant interface, not disease management in general
- Real world Utilization of transplant in AML CR1 in ANZ- **Need to improve transplant utilization (2013-2018)**

	Total Participants	CR/CRi	Transplanted from CR/CRi
Intermediate	386	344(88%)	80(23%)
Adverse	112	79(71%)	40(51%)

Thiagarajah N, Bajel A et al ASH 2024

How - Built by consensus, graded by evidence

Following ANZTCT's policy for Consensus Practice / Position Statement development

1

All centres invited

Every Australian and New Zealand bone marrow transplant centre was invited to participate; the authorship spans all Australian states and NZ.

2

Literature reviewed

Relevant evidence was identified and synthesised by the full authorship group across genomics, MRD, novel agents, and transplant outcomes.

3

Consensus recommendations

Recommendations were developed through group discussion and agreed by consensus — not derived from a single trial or dataset.

4

NHMRC grading applied

Where appropriate, NHMRC levels of evidence and grades (B–D) were assigned; ungraded statements reflect standard agreed practice.

WHAT

The practice recommendations

Inputs that drive every transplant decision

Patient selection is increasingly individualised rather than protocol-driven$

1

Disease risk

ELN 2022/2024 classification from comprehensive molecular profiling, MRD

2

Disease State

CR1 vs R/R

3

Patient fitness

Comorbidity and organ-function assessment for transplant risk

4

Donor availability

Matched sibling, unrelated, haploidentical, or cord options

.

The modern diagnostic backbone

Genomic profiling and MRD assessment now underpin every downstream decision

Genomic profiling

DNA- and RNA-based assays now routinely detect **NPM1, FLT3-ITD/TKD, IDH1/2, TP53, KMT2A** and cryptic fusions — underpinning ELN risk classification and induction choice. Novel risk factors – UBTF tandem duplications..

Recommendation — NHMRC Grade B

Conduct comprehensive molecular profiling to stratify risk and identify actionable mutational targets.

MRD assessment

Multiparametric flow cytometry, quantitative PCR, fusion-transcript PCR, and NGS-based MRD **give real-time risk assessment** and inform the timing and intensity of transplant.

Recommendation — NHMRC Grade B

Apply guideline-directed MRD assessment to measure response depth and enable timely transplant referral.

Upfront therapy — older patients

Low-intensity regimens have expanded who can reach remission — and transplant eligibility

66%

vs 28%

CR/CRi rate

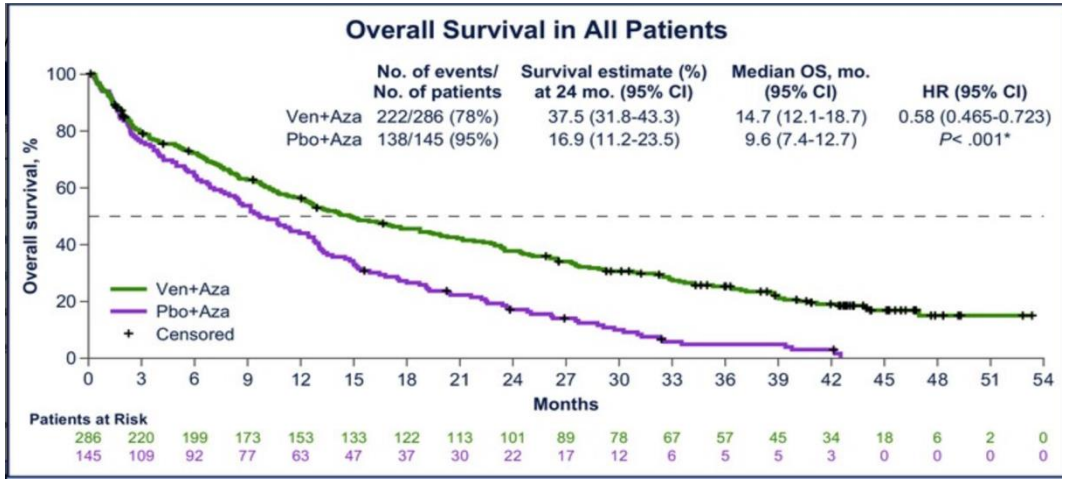
VEN–AZA vs AZA alone

14.7

vs 9.6 mo

Overall survival

VEN–AZA vs AZA alone



VIALE-A (phase III): venetoclax–azacitidine vs azacitidine monotherapy in newly diagnosed, treatment-ineligible AML.

- High initial response with VEN–AZA, but relapse remains common — allo-HSCT should be considered for eligible patients

Pratz KW et al Am J Hematol 2024

Upfront therapy — fit patients

Intensive chemotherapy remains the backbone — increasingly paired with targeted agents

1

FLT3 inhibitors

FLT3 inhibitors + intensive chemotherapy deepens remission and improves survival

2

VEN–AZA vs intensive chemo

Recent randomised trials in selected fit cohorts suggest improved event-free survival with VEN-based regimens, blurring the fit/unfit divide.

3

CPX-351

Improves OS in secondary/therapy-related AML -

Recommendation — NHMRC Grade B

Tissue typing and early transplant referral should be considered for all eligible patients with intermediate or adverse-risk AML, regardless of induction intensity.

Relapsed / refractory AML — bridging to transplant

Allo-HSCT remains the only route to cure despite novel agents achieving response

Gilteritinib	*ADMIRAL trial*	Significant OS improvement vs salvage chemo in FLT3-mutated R/R AML — now standard of care.
Revumenib	*AUGMENT-101 (I/II)*	63.2% overall response, 22.8% CR, 68.2% MRD-negative CR in NPM1/KMT2A-driven disease; FDA approved.
Ziftomenib	*KOMET-001*	35% overall response; 67% of those reaching CR were MRD-negative. FDA approved for NPM1-mutated R/R AML.
VEN-based salvage	—	

Who benefits

CR1

Adverse-risk AML derives clear benefit; intermediate-risk is refined by MRD; favourable-risk generally managed without transplant unless MRD persists.

TP53-mutated

Heterogeneous and highest-risk — poorer outcomes, but allo-HSCT remains the only potentially curative option. Should not be excluded on biology alone.

CR2

Typically recommended when feasible; prognosis is inferior to CR1, reinforcing early donor identification at initial diagnosis.

R/R AML

The ASAP trial found no survival advantage for remission induction before conditioning over immediate sequential conditioning — though logistics still limit uptake.

MRD and Transplant

Prognostic before transplant, decision-guiding at conditioning, and a surveillance tool after

BEFORE

MRD positivity before allo-HSCT is consistently linked to higher relapse risk and lower survival, regardless of morphological remission.

AT CONDITIONING

MRD-positive patients may benefit from myeloablative conditioning and planned post-transplant monitoring

AFTER

Post-transplant MRD complements chimerism analysis to flag imminent relapse

Recommendation

MRD status should guide, but never delay or deny, allo-HSCT — reducing MRD pre-transplant should be considered when options accessible and feasible, not a precondition.

Minimising toxicity before conditioning

Washout periods are agent-specific — balancing disease control against organ recovery

Agent	Recommended washout	Rationale
Venetoclax	**7–10 days**	Based on ~26h terminal half-life; adjusted for cytopenias and marrow recovery.
CPX-351	**4–6 weeks**	After count recovery; adjusted for comorbidities and donor availability.
FLT3 inhibitors	**~7 days**	Varies with drug pharmacokinetics and institutional protocol.
Gemtuzumab ozogamicin	**2–3 months**	Longer washout to mitigate sinusoidal obstruction syndrome risk; ursodeoxycholic acid prophylaxis recommended.

Alongside washout: proactively optimise end-organ function [Grade B] and mitigate infection risk with early surveillance and prophylaxis [Grade B].

Transplant timing & conditioning intensity

Parallel planning — donor search starts during induction, not after

ANZTCT / NBCR (2013–2018)

2.1 mo
(0.7-5.3)

median time to matched sibling allo-HSCT after CR1

3.7 mo
(0.7– 11.5)

median time to unrelated donor allo-HSCT after CR1

Timing Matters

Unnecessary delay — chasing deeper MRD response, or donor logistics

Conditioning intensity is individualised

Reduced-intensity

Older patients or those with comorbidities

Myeloablative

Fit patients with persistent MRD or adverse-risk biology, if non-relapse mortality risk is acceptable

Factors weighed: fitness, comorbidities, disease risk, and MRD status — together,

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Special populations & coordinated care

Paediatric & AYA patients

- Distinct genomic landscape, lower comorbidity burden — fitness rarely limits transplant
- Greater donor availability: haploidentical (parent) and cord blood used more readily
- MRD negativity is not a strict requirement — long-term remission is possible with positive MRD

Multidisciplinary coordination

- Early haematologist – transplant centre collaboration avoids missed windows, especially after rapid low-intensity remission
- Parallel donor identification and treatment planning reduces unnecessary delay
- Regional & regulatory: PBS/TGA (Australia) and Medsafe/Pharmac (NZ) approval timelines may lag emerging trial data
- Access to standardised MRD testing and genomic profiling varies by institution — pathways must adapt pragmatically

Next Steps and Future opportunities

- Manuscript submitted
- Future opportunities for consideration
    - Post transplant monitoring and intervention strategies

Acknowledgements

All my Co –authors

Prof Nada Hamad

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