Identification and management of children with cancer and low-risk febrile neutropenia

1. Background

In children with cancer and fever and neutropenia (FN) an infection or serious medical complication is documented in less than half of all episodes. The risk of infection or complication may be assessed using the 'AUS-rule' that has been validated in and Australian paediatric FN study. Children with low-risk FN may be managed safely at home with oral or intravenous antibiotics. This has been shown to improve quality of life and reduce healthcare expenditures.

2. Risk stratification

The following criteria below need to be fulfilled to be suitable for assessment with the 'AUS-rule'.

Table 1. Suitability for risk stratification

Criteria	Eligible	Not eligible
Neutropenia ANC of < 1.0 X 10^9/L	☐ Yes	☐ No
Fever of ≥ 38.0^{o}C	☐ Yes	☐ No
Cancer or haematological malignancy	☐ Yes	☐ No
All criteria needs to be fulfilled to continue with risk stratification		

2.1 AUS-rule clinical decision rule

All children admitted to hospital with fever (≥ 38.0^{o}C) and neutropenia (ANC <1.0x10^9 cells/L) should be risk stratified using the AUS-rule (Table 2). The risk score must be documented in the medical record. This includes patients who may already be admitted and who develop FN while an inpatient and who are not already on any antimicrobials (excluding prophylactic antimicrobials). The AUS-rule score is based on the FBE blood results at the time of the initial onset of fever. The AUS-rule predicts microbiologically or clinically defined bacterial infections. The AUS-rule score can assist clinicians in determining when the patient can be safely transferred to home-based FN care.

Table 2: AUS-rule variables and score

AUS-rule Variables	Yes	No
Preceding chemotherapy more intensive than ALL maintenance	☐ 1	☐ 0
Total white cell count < 0.3 x10^9/L	☐ 1	☐ 0
Platelet <50 x10^9/L	☐ 1	☐ 0
TOTAL SCORE		
Score 0 = This patient is **very-low risk** for a bacterial infection. If they are clinically stable and fulfil the HITH safety-net criteria then transfer to the 'Low-risk FN program' after a **minimum of 4 hs of observation.**		
Score 1 = This patient is **low risk** for a bacterial infection. If they are clinically stable and fulfil the HITH safety-net criteria then transfer to the 'Low-risk FN program' **within 24 hs.**		
Score 2 = This patient is **moderate risk** for a bacterial infection. If they are clinically stable and fulfil the HITH safety-net criteria then *consider* transfer to the low-risk FN program after a **minimum of 24 hs inpatient observation**.		
Score 3 = This patient is **higher risk** for a bacterial infection. If they are clinically stable and fulfil the HITH safety-net criteria then ***consider*** transfer to the low-risk FN program after a **minimum of 36-48 hs inpatient observation**.		

3. Eligibility for early transfer to Hospital-In-The-Home (HITH)

Depending on the AUS-rule score, patients with FN may be suitable for transfer to HITH within 4 to 24 hours of admission (Table 3). The patient will require outpatient monitoring and antibiotics (Table 4), via HITH, until resolution of fever and evidence of marrow recovery (see 5.2).

Table 3: Eligibility criteria for early transfer to HITH (must be YES to all to proceed to HITH):

Criteria	Eligible	Not eligible
Disease status. Leukaemia/lymphoma in remission (as per last BMA) or solid tumour stable/responding (as per oncologist)	☐ Yes	☐ No
Disease group. Not any of: ALL induction, infant ALL, AML, post HSCT, congenital immunodeficiency, aplastic anaemia	☐ Yes	☐ No
Expected duration of neutropenia < 7 days	☐ Yes	☐ No
No confirmed focus of infection requiring inpatient care*	☐ Yes	☐ No
No medical complication requiring inpatient care**	☐ Yes	☐ No
No severe sepsis at FN presentation***	☐ Yes	☐ No
No active infection with multi-drug resistant bacteria (ie, MRSA, VRE, MDRGN)	☐ Yes	☐ No
Availability of a 24 hour caregiver	☐ Yes	☐ No
Good education of patient and carer on reportable symptoms	☐ Yes	☐ No
Availability of a telephone (with credit)	☐ Yes	☐ No
Availability of 24 hour phone advice/emergency department review from treating hospital	☐ Yes	☐ No
Within 1-hour of an emergency department or treating hospital	☐ Yes	☐ No
Treating team preference	☐ Yes	☐ No
No previous history of non-compliance with medical care	☐ Yes	☐ No

*including, *but not limited to*, CVAD site infection, cellulitis, perianal cellulitis or pain, pneumonia, colitis.

**including, *but not limited to*, pain requiring intravenous analgesia, poor oral intake or excessive loss requiring intravenous hydration; respiratory distress or oxygen requirement; pulmonary infiltrates on CXR.

***severe sepsis includes any of (i) altered conscious state, (ii) inotrope requirement, (iii) fluid bolus requirement >40ml/kg or (iv) respiratory report requirement

Table 4. Intravenous and oral antibiotic options for HITH

No beta-lactam allergy Piperacillin-tazobactam 400mg/kg/day (maximum16,000mg of piperacillin every 24 hours) intravenous continuous infusion. ***Pharmacy must be notified by 10am the morning of discharge to make up infusion the same day*** For patients who are well (inc. no mucositis, vomiting or diarrhoea) oral Augmentin and Ciprofloxacin can be considered instead of intravenous antibiotics. The patient should have a dose of both oral antibiotics prior to transfer home to ensure they are tolerated.
Non-life threatening beta-lactam allergy (rash): Ceftazidime 150mg/kg/day (maximum 6,000mg every 24 hours) intravenous continuous infusion. For patients who are well (inc. no mucositis, vomiting or diarrhoea) oral Clindamycin and Ciprofloxacin can be considered instead of intravenous antibiotics. The patient should have a dose of both oral antibiotics prior to transfer home to ensure they are tolerated. **Life-threatening beta-lactam allergy (anaphylaxis):** If requiring IV antibiotics manage as inpatient. For patients who are well (inc. no mucositis, vomiting or diarrhoea) oral Clindamycin and Ciprofloxacin can be considered instead of intravenous antibiotics. The patient should have a dose of both oral antibiotics prior to transfer home to ensure they are tolerated.

5. HITH schedule, key responsibilities and patient point of contact

Once patient is assessed as low risk and has met all criteria for early transfer, they are referred to HITH. Transfer to HITH is recommended after a minimum period of in-hospital observation as per the AUS-rule score. See Table 5 for HITH schedule.

5.1 HITH schedule and key responsibilities

The following is a recommended schedule for HITH visits and interventions (see Table 5).

- Daily visits (Day 0 is day of transfer to HITH) until suitable for discharge (see 5.2)
- Interventions to be undertaken during home visit;
    - Administer intravenous antibiotic (if applicable)
    - Blood specimens taken - FBE (all) and U&E, LFTs (as required)
    - Home assessment chart reviewed / discussed (refer to home assessment chart), including temperature, oral intake / hydration, bowel patterns
- Patients' blood results monitored daily by {Insert clinician/role responsible} who will liaise with the oncology medical treating team.
- Patient/family contacted by telephone by {Insert clinician/role responsible}at least once during the HITH admission for a phone review and discussion of results
- If absolute neutrophil count (ANC) remains < 0.2 x 10^9/L on Day 4, the patient must have medical review on Day 5 and decision made for readmission or ongoing HITH follow up.

5.2 HITH discharge criteria

Patients can be discharged from HITH when all of the following are fulfilled:

- clinically well
- no documented infection requiring ongoing antibiotics
- afebrile for >24 hours
- evidence of marrow recovery (as judged by the treating clinician), including a post nadir ANC of at least >0.2 X 10^9 cells/L and platelet recovery

Table 5: HITH schedule

Day	Appointments / interventions	Responsibility
0 (day of transfer	Bloods reviewed prior to hospital discharge HITH appointments arranged Educational material / self-assessments (temperature monitoring) provided to patient Readmission letter provided to patient	{Insert clinician/role responsible} *and* Treating team
1	Home visit for: -IV antibiotics -Observations and review home assessment chart -Blood tests {Insert clinician/role responsible} to update treating team	{Insert clinician/role responsible}
	Review of blood results and action as required	{Insert clinician/role responsible} *and* Treating team
2	Home visit for: -IV antibiotics -Observations and review home assessment chart -Blood tests {Insert clinician/role responsible} to update treating team	{Insert clinician/role responsible}
	Review of blood results and action as required	{Insert clinician/role responsible} *and* Treating team
3	Home visit for: -IV antibiotics -Observations and review home assessment chart -Blood tests {Insert clinician/role responsible} to update treating team	{Insert clinician/role responsible}
	Review of blood results	{Insert clinician/role responsible} *and* Treating team

	Telephone follow up Blood results discussed	{Insert clinician/role responsible} *or* Treating team
4	Home visit for: -IV antibiotics -Observations and review home assessment chart -Blood tests {Insert clinician/role responsible} to update treating team *NB. If ANC < 0.2 x 10^9 /L and still on program, patient must have medical review on Day 5 and decision made for readmission or ongoing HITH follow up.*	{Insert clinician/role responsible}
	Review of blood results	{Insert clinician/role responsible} *and* Treating team
	Telephone follow up Blood results discussed	{Insert clinician/role responsible} *or* Treating team
5-7	If ANC remains < 0.2 X 10^9 cells/L patient to attend hospital for medical review and decision made for readmission or ongoing HITH follow up.	{Insert clinician/role responsible} *and* Treating team

5.3 Patient point of contact

The hospital contact number for all patients admitted on the low-risk FN program is {insert hospital contact details} available 24 hours per day. The call will be managed by the {insert person/team responsible} during business hours and by the {insert person/team responsible after hours}. Patient queries should be managed according to the local policy.

6. Patient resources

Patient resources should include:

- HITH appointments
- Pathology requests
- Educational material:
  - home observation and assessment chart with instructions for use
  - when to call the hospital and when to re-present to hospital
  - hospital contact numbers
  - letter for presentation to an emergency department including description of medical history, recent treatment received and current situation
- Ensure patient has a thermometer

7. Medical reviews and re-admission

A medical review and/or re-admission for in hospital care may be required for some patients on the low-risk FN program. All patients/families should receive education on symptoms and signs for review or readmission, prior to transfer to HITH.

Patients with the following criteria will require a medical review and/or readmission for inpatient care:

- Recurrent or persistent fever (> 48hrs from presentation) or new fever after being afebrile for 24 hours
- Feeling unwell / new signs and symptoms
- Significant decrease in oral intake (i.e. < 50% baseline) or significantly increased losses (vomiting or diarrhoea)
- Positive blood culture result (reported after patient hospital discharge) or other infection requiring inpatient care
- Pain: severe or persistent
- Inability to continue with oral antibiotics if applicable (i.e. allergy, vomiting, severe diarrhoea or patient refusal)
- Chills/rigors/shaking

Patients requiring urgent review are required to present to the Emergency Department (ED). The {insert person/team/department} is responsible for notifying the ED of the patient expect. The patient will be managed according to triage category. The Oncology team is responsible for reviewing the patient in ED. Patients on IV antibiotics with signs of sepsis should receive a stat dose of an aminoglycoside +/- Vancomycin (as per your local policy)