EFFICACY IN Ph+ RELAPSED OR REFRACTORY B-ALL

BLINCYTO® WAS STUDIED IN AN OPEN-LABEL, MULTICENTRE, SINGLE-ARM PHASE II STUDY IN PATIENTS WITH Ph+ RELAPSED OR REFRACTORY B-ALL (ALCANTARA)[1]

Martinelli G *et al. J Clin Oncol* 2017; 35:1795–802.

ALCANTARA STUDY DESIGN[1]

Adults ≥18 years of age with relapsed or refractory Ph+ B-ALL:

- Relapsed after or refractory to at least 1 second- or later-generation TKI **OR**
- Intolerant to second- or later-generation TKI and intolerant or refractory to imatinib

WITH

- >5% bone marrow blasts
- ECOG performance status ≤2

AND WITHOUT

- History or presence of clinically relevant CNS pathology (eg, epilepsy, stroke, dementia)
- Active acute or chronic GVHD or systemic treatment for GVHD within 2 weeks before treatment start
- Allogeneic HSCT within 12 weeks of starting treatment in this trial

BLINCYTO® single-agent immunotherapy

- cIV infusion for 2 induction cycles followed by up to 3 consolidation cycles
- **Treatment cycle:** 4 weeks on drug, 2 weeks off
- **Dosing:** 9 mcg/day on Days 1-7 of Cycle 1 and 28 mcg/day on subsequent days

Adapted from Martinelli *et al.* 2017.[1]
‡Patients who achieved CR or CRh within the first two cycles could receive up to three additional cycles.

STUDY ENDPOINTS[1]

Primary endpoint	• CR or CRh during the first two cycles
Major secondary endpoints	• MRD response rate (MRD negativity) • Rate of allogeneic HSCT • RFS • OS

CR was defined as ≤5% blasts in the bone marrow, no evidence of disease, and full recovery of peripheral blood counts (platelets >100,000/mcL and ANC >1,000/mcL).

CRh was defined as ≤5% blasts in the bone marrow, no evidence of disease, and partial recovery of peripheral blood counts (platelets >50,000/mcL and ANC >500/mcL).

A stringent definition of complete MRD response (no amplification of BCR-ABL by PCR with 10^{-5} sensitivity) was used.[1]

Reference: 1. Martinelli G *et al. J Clin Oncol* 2017; 35:1795–802.

EFFICACY IN Ph+ RELAPSED OR REFRACTORY B-ALL

PATIENT POPULATION[1]

BLINCYTO® WAS STUDIED IN A POOR PROGNOSIS Ph+ RELAPSED OR REFRACTORY B-ALL POPULATION[1]

BASELINE DEMOGRAPHIC AND DISEASE CHARACTERISTICS	
Sex, n (%)	
Male	24 (53)
Median age (range), years	55 (23-78)
Age, n (%)	
18 to <55 years	22 (49)
≥55 years	23 (51)
Prior TKI exposure, n (%)	45 (100)
Dasatinib	39 (87)
Imatinib*	25 (56)
Ponatinib	23 (51)
Nilotinib	16 (36)
T315I mutation, n (%)	10 (27)†
Prior allogeneic HSCT, n (%)	20 (44)
Median baseline bone marrow blast, % (range)	80 (6-98)

84% of patients had received ≥2 prior TKI treatments.

51% of patients were resistant or intolerant to ponatinib.

27% of patients had the T315I mutation.

*One patient was resistant to imatinib and never exposed to another TKI (protocol deviation).
†37 patients had evaluable mutational analysis data.

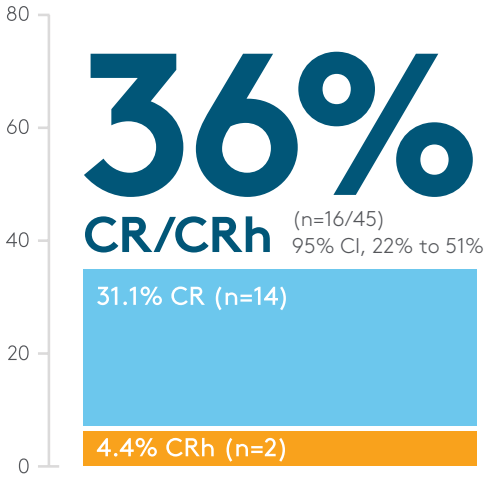
Reference: 1. Martinelli G *et al. J Clin Oncol* 2017; 35:1795–802.

EFFICACY IN Ph+ RELAPSED OR REFRACTORY B-ALL

BLINCYTO® INDUCED CR/CRh IN MORE THAN ONE THIRD OF PATIENTS[1]

PRIMARY ENDPOINT: CR/CRh RATE WITHIN THE FIRST 2 BLINCYTO® TREATMENT CYCLES[1]

Primary Endpoint: CR/CRh Rate Within 2 Treatment Cycles



2 additional patients achieved CR with an incomplete haematologic recovery.

Consistent Response Across Subgroups[1]

40% (n=4/10) CR/CRh among patients with **T315I mutation**

47% (n=8/17) CR/CRh among patients treated with **≥3 prior second- or later-generation TKIs**

35% (n=8/23) CR/CRh among patients with **ponatinib resistance/intolerance**

44% of responders (n=7/16) proceeded to transplant.[1]

Adapted from Martinelli *et al.* 2017.[1]

Reference: 1. Martinelli G *et al. J Clin Oncol* 2017; 35:1795–802.

EFFICACY IN Ph+ RELAPSED OR REFRACTORY B-ALL

THE MAJORITY OF PATIENTS WHO ACHIEVED CR/CRh WITH BLINCYTO® HAD A COMPLETE MRD RESPONSE[1]

88%
(n=14/16)

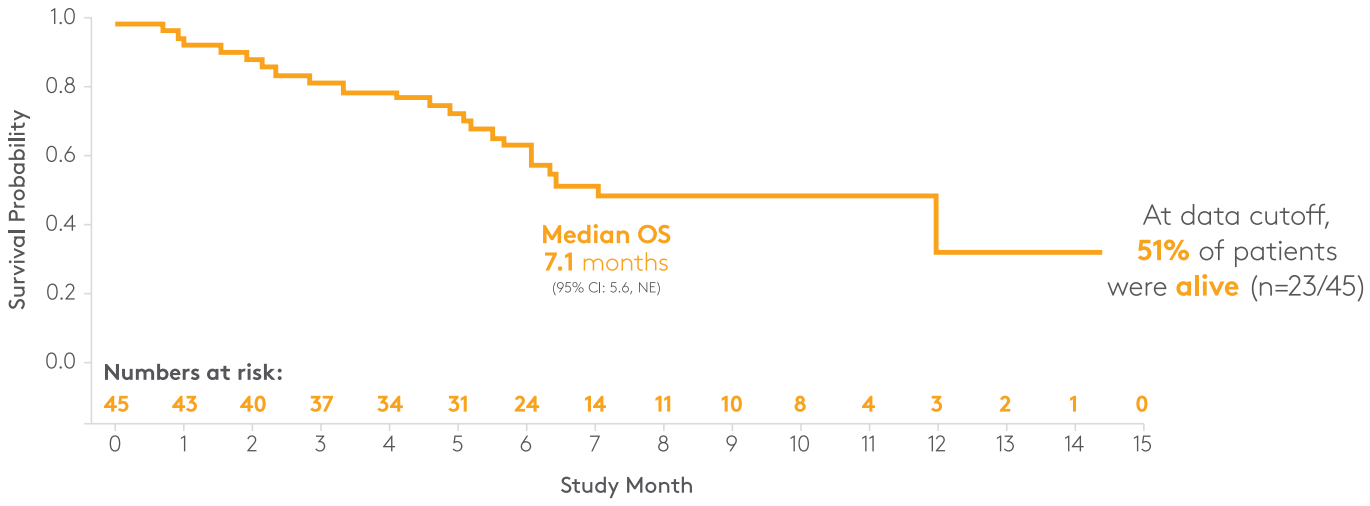
of patients with CR/CRh were
MRD negative within 2 treatment cycles.[1]

- Complete MRD response (MRD negativity) was defined as no RT-PCR amplification of BCR-ABL at a sensitivity of 10^{-5}.[1]

Haematologic and molecular responses were independent of mutational status, including presence of the T315I mutation.[1]

MEDIAN OS FOR ALL PATIENTS WAS 7.1 MONTHS[1]

OS among patients treated with BLINCYTO®[1]



Adapted from Martinelli *et al.* 2017.[1]

Median RFS among patients who achieved CR/CRh was 6.7 months (95% CI, 4.4 to NE).[1]

NE: not evaluable.

Reference: 1. Martinelli G *et al. J Clin Oncol* 2017; 35:1795–802.

SAFETY IN Ph+ RELAPSED OR REFRACTORY B-ALL

BLINCYTO®: CHEMOTHERAPY-FREE IMMUNOTHERAPY WITH A MANAGEABLE TOLERABILITY PROFILE[1]

ADVERSE EVENTS AND NEUROLOGIC EVENTS (REGARDLESS OF CAUSALITY)[1]

	GRADE					
	Any		3		4	
Event	**No.**	**%**	**No.**	**%**	**No.**	**%**
Patients with adverse events	**45**	**100**	**33**	**73**	**16**	**36**
Adverse events of grade ≥3 occurring in ≥5% of patients*						
Pyrexia	26	58	5	11	0	0
Febrile neutropenia	18	40	12	27	0	0
Headache	14	31	3	7	0	0
Anaemia	13	29	7	16	1	2
Thrombocytopenia	10	22	5	11	7	16
Pain	7	16	4	9	0	0
Increased AST	6	13	3	7	2	4
Increased ALT	5	11	5	11	0	0
Device-related infection	5	11	3	7	0	0
Neutropenia	3	7	0	0	3	7
Patients with neurologic events	**21**	**47**	**3**	**7**	**0**	**0**
Neurologic events occurring in two or more patients						
Paresthesia	6	13	0	0	0	0
Confused state	5	11	0	0	0	0
Dizziness	4	9	0	0	0	0
Tremor	4	9	0	0	0	0
Aphasia	2	4	1	2	0	0
Cerebellar syndrome	2	4	0	0	0	0
Memory impairment	2	4	0	0	0	0
Nervous system disorder	2	4	1	2	0	0

*Cutoff based on grade ≥3 adverse events.
Adapted from Martinelli *et al.* 2017.

Please see Adverse Events Management section for further details.

- The most common treatment-emergent adverse events with BLINCYTO® included pyrexia (58%), febrile neutropenia (40%), and headache (31%)[1]
- 5 (11%) fatal treatment-emergent adverse events occurred, 1 of which was considered related to BLINCYTO® treatment (septic shock)[1]

Reference: 1. Martinelli G *et al. J Clin Oncol* 2017; 35:1795–802.

BLINCYTO®
(blinatumomab)

For more information on BLINCYTO® or to report any adverse events or product complaints involving BLINCYTO® please contact Australia Medical Information on 1800 803 638

PBS Information: Section 100 listed. Authority required.
Refer to PBS Schedule for full Authority listing.

***WARNING*:** *The following have occurred in patients receiving BLINCYTO®:*
• Cytokine Release Syndrome, which may be life-threatening or fatal • Neurological toxicities, which may be severe, life-threatening, or fatal • Reactivation of JC viral infection
Interrupt or discontinue BLINCYTO® as recommended if any of these adverse events occur
(See Section 4.4 Special warnings and precautions for use and Section 4.2 Dose and method of administration).

REFER TO FULL PRODUCT INFORMATION BEFORE PRESCRIBING; AVAILABLE FROM AMGEN AUSTRALIA PTY LTD, PH: 1800 803 638 OR AT WWW.AMGEN.COM.AU/BLINCYTO.PI

For more information about BLINCYTO® or to report an adverse event or product complaints about BLINCYTO®, please contact Amgen Medical Information on 1800 803 638.

BLINCYTO® Minimum Product Information: Indication: treatment of relapsed or refractory (R/R) B-cell precursor acute lymphoblastic leukaemia (ALL); treatment of minimal residual disease (MRD) positive ALL in patients in complete haematological remission. **Contraindications:** hypersensitivity to blinatumomab, CHO-derived proteins or any excipient. **Precautions:** neurologic events; increased risk for serious infections; cytokine release syndrome; infusion reactions; tumour lysis syndrome, pancreatitis. Management of these adverse reactions may require interruption or discontinuation of treatment. Neutropenia and febrile neutropenia; elevated liver enzymes; leukoencephalopathy; medication errors – strictly follow preparation and administration instructions. Pregnancy Category: C. Use contraception during and for 48 hours after treatment. Discontinue breast-feeding during and for at least 48 hours after treatment. Do not use recommended adult fixed dose in paediatric patients. No data in patients aged less than 28 days. **Interactions:** low potential of clinically meaningful drug interaction with BLINCYTO® mediated cytokine elevation. Vaccination with live viral vaccines not recommended 2 weeks prior to or during treatment, and until recovery of B lymphocytes to normal range following last treatment cycle. **Adverse Reactions:** Common: infections, pyrexia, infusion-related reactions, headache, anaemia, febrile neutropenia, neutropenia, thrombocytopenia, oedema, increased liver enzymes, fatigue, nausea, tremor, hypokalaemia, diarrhoea, chills. See also Precautions for serious adverse reactions. **Dosage & Administration:** R/R ALL: Single cycle is 4 weeks continuous intravenous (cIV) infusion then 2 week treatment free interval. *For patients greater than or equal to 45 kg (fixed dose)*: Cycle 1 – starting dose 9 micrograms/day for days 1-7, then 28 micrograms/day for days 8-28. All other cycles 28 micrograms/day for 4 weeks. For patients less than 45 kg (body surface area based dose): Cycle 1 – starting dose 5 micrograms/m^2/day for days 1-7 (do not exceed 9 micrograms/day), then 15 micrograms/m^2/day (do not exceed 28 micrograms/day); all other cycles, 15 micrograms/m^2/day (do not exceed 28 micrograms/day). For maintenance, 28 day cIV infusion, then 56 days treatment free. Hospitalise at least first 9 days of Cycle 1 and first 2 days of Cycle 2. Supervision or hospitalisation for other cycle starts and reinitiation. Adults: premedicate with 20 mg IV dexamethasone prior to initiation of each cycle. Intrathecal chemotherapy prophylaxis recommended before and during therapy. Treat with dexamethasone (≤ 24 mg/day) if high tumour burden. Paediatrics: premedicate with dexamethasone 10 mg/m2 (not to exceed 20 mg) oral or IV 6 to 12 hours prior to start of BLINCYTO® (Cycle 1 day 1), followed by premedication with dexamethasone 5 mg/m^2 oral or IV within 30 minutes of start of BLINCYTO® (Cycle 1 day 1). **MRD+ ALL:** 28 day cIV infusion then 14 days treatment free, for up to 4 cycles; premedicate with prednisone 100 mg IV or equivalent 1 hour prior to start of BLINCYTO® each cycle; hospitalise first 3 days Cycle 1 and first 2 days Cycle 2, supervise/hospital for subsequent cycle starts and reinitiation – see full PI. R/R & MRD+ ALL – Interrupt BLINCYTO® if grade 3 neurological events, Cytokine Release Syndrome or other clinically relevant adverse reactions occur see full PI.

BLINCYTO®
(blinatumomab)

AMGEN®