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- The prognosis for adults with relapsed or refractory B-cell precursor acute lymphoblastic leukemia (BCP-ALL) is poor.
- Minimal/measurable residual disease (MRD) positivity (MRD+) is the strongest predictor of relapse.
- Blinatumomab, a CD3/CD19-directed BITE® (bispecific T-cell engager) molecule, is an effective treatment for patients with MRD+ BCP-ALL.¹⁻⁵
 - Blinatumomab is administered as a continuous intravenous infusion (cIV) 28 days per cycle. Severe adverse events (AEs) such as cytokine release syndrome (CRS) and neurologic toxicity (NT) may occur; thus, hospitalization is recommended for the first 3 days of cycle 1 and the first 2 days of cycle 2 for patients with MRD+ disease.
 - However, the incidence of severe AEs is low in patients with MRD+ BCP-ALL (CRS: 2%; NT: 13%).⁴
- The use of effective remote digital monitoring devices can ensure that blinatumomab can be safely administered for the entire 28-day cIV cycle in an outpatient setting.

Table 1. Key Inclusion Criteria

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Patient

- Age ≥ 18 years, BCP-ALL in complete remission (CR) with MRD+ disease (MRD of $\geq 0.1\%$ blasts), Philadelphia (Ph)+ or Ph–, with CR defined as:
 - $<5\%$ bone marrow blasts
 - Absolute neutrophil count $\geq 1.0 \times 10^9/L$
 - Platelets $\geq 50 \times 10^9/L$, transfusion permitted
 - Hemoglobin level ≥ 9 g/dL (90 g/L), transfusion permitted
- Normal renal and hepatic function
- Eastern Cooperative Oncology Group performance status of 0 or 1
- Can comply with use of the Current Health Wearable Monitoring System (CHWMS)
- Adequate cellular or Wi-Fi service during monitoring
- Stay within a 1-hour drive of an advanced medical care facility for the duration of the monitoring period

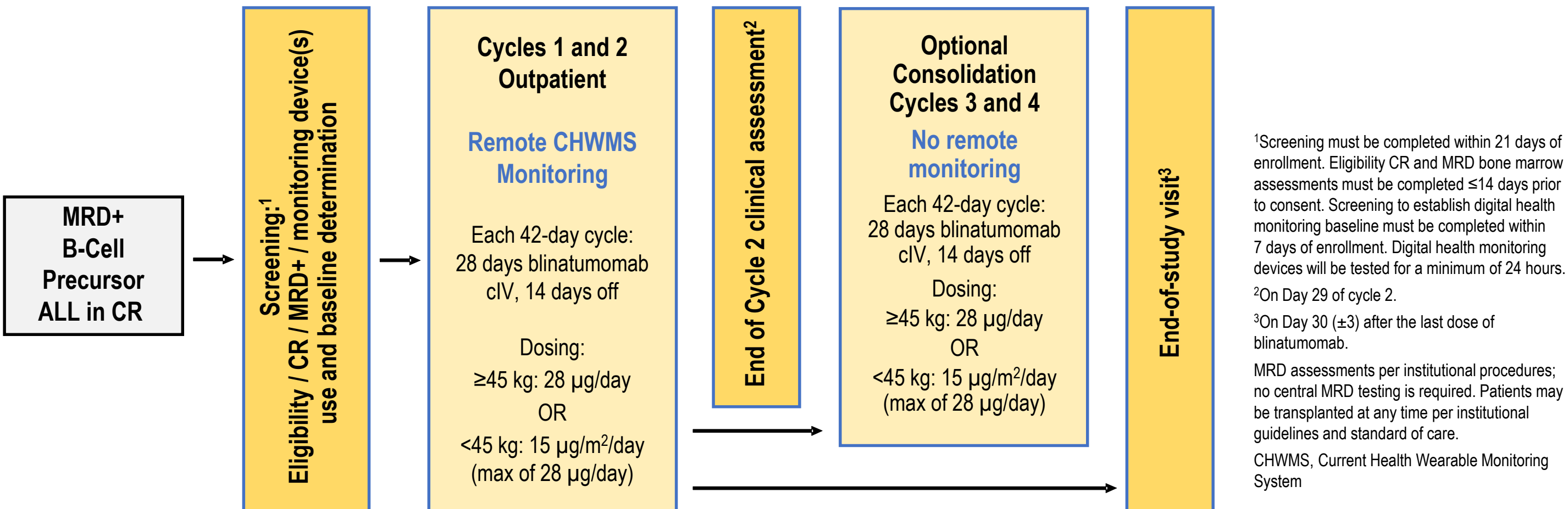
Caregiver

- Adult with access to transportation present 24 hours/day for the entire monitoring period
- Able to participate in the health management of the patient and to assist with the requirements of remote digital monitoring devices

CNS, central nervous system; CSF, cerebrospinal fluid; HBV, hepatitis B virus; HCV, hepatitis C virus; HIV, human immunodeficiency virus. *Such as seizure, paresis, aphasia, severe brain injuries, dementia, Parkinson's disease, psychosis, movement disorders. †If leukemic blasts are found in the CSF, patients must receive intrathecal treatment and demonstrate negative CSF before enrollment.

- Adult patients (n = 45) with BCP-ALL in complete remission and MRD+ ($\geq 0.1\%$ blasts) are being enrolled at 25 planned treatment sites (Amgen NCT04506086).
- Patient suitability for blinatumomab and outpatient monitoring is established.

Figure 1. Study Design



- Patients will receive 2–4 cycles of blinatumomab. The mandatory device monitoring period (MDMP) will be during the first 3 days of cycle 1 and the first 2 days of cycle 2 only.
- Cycles are initiated in the outpatient setting. Remote digital monitoring devices are activated and attached, and patients are sent home.
- Once home, patients set up the home connectivity hub and real-time remote data transfer to the healthcare provider (HCP) begins.
- The devices are worn continuously, 24 hours a day, during the MDMP.
- The Current Health Wearable Monitoring System (CHWMS) provides heart rate (HR), respiratory rate (RR), and continuous oxygen saturation (SpO₂); an axillary temperature sensor is worn and provides continuous temperature.
- Patient-specific requirements include:
 - Manually measure blood pressure every 3–6 hours around the clock.
 - Has an integrated mobile device (tablet), with device information and instructions for set up, to initiate contact with the HCP if needed, to receive video communication from the HCP as needed, and to complete the electronic patient-reported outcomes (ePROs).
- HCP-specific requirements include:
 - Has a mobile device (smart phone) and receives vital signs as a constant live feed transmitted from the CHWMS device. The CHWMS platform generates a loud audible alert based on pre-specified vital sign alarming thresholds or if there is an interruption in data transfer. HCP may initiate direct audio and video contact with the patient, assess the patient's condition, and make an appropriate intervention. Video calls to assess for neurotoxicity are to be made at a minimum of every 12 hours.
 - HCP may also initiate patient contact in the absence of an alert.

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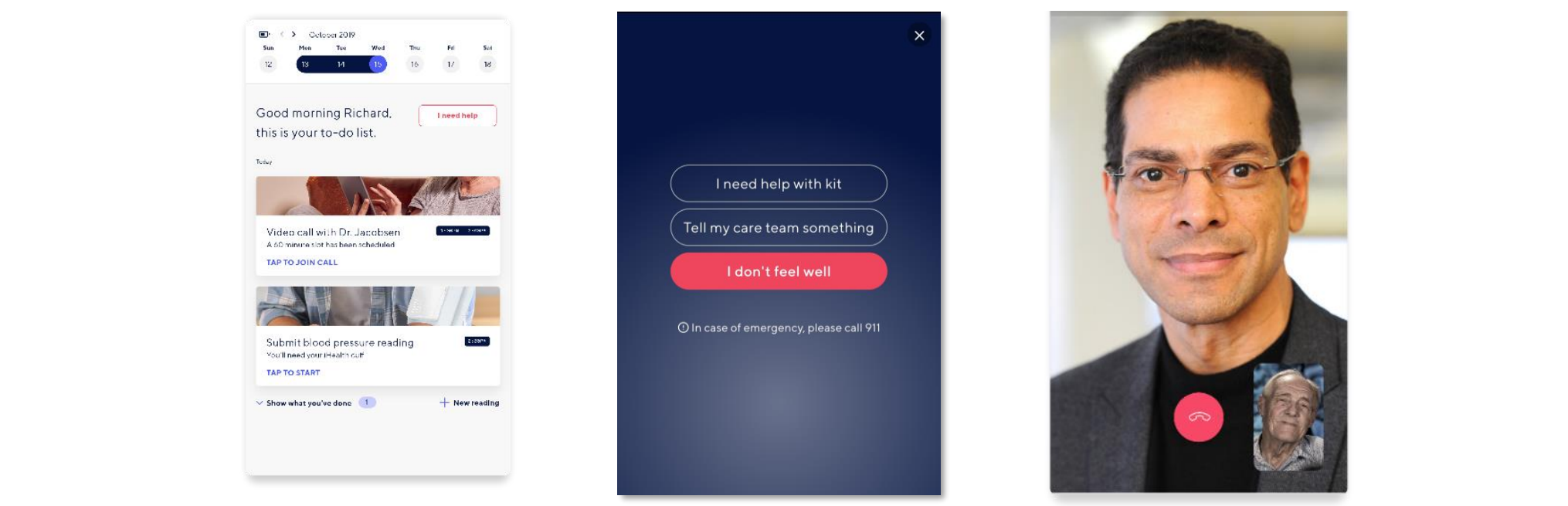
- Trial enrollment is underway.
- This study will generate feasibility data on the effectiveness of home monitoring and safety of outpatient administration of blinatumomab infusion in patients with MRD+ BCP-ALL.

Figure 2. Current Health Wearable Monitoring System



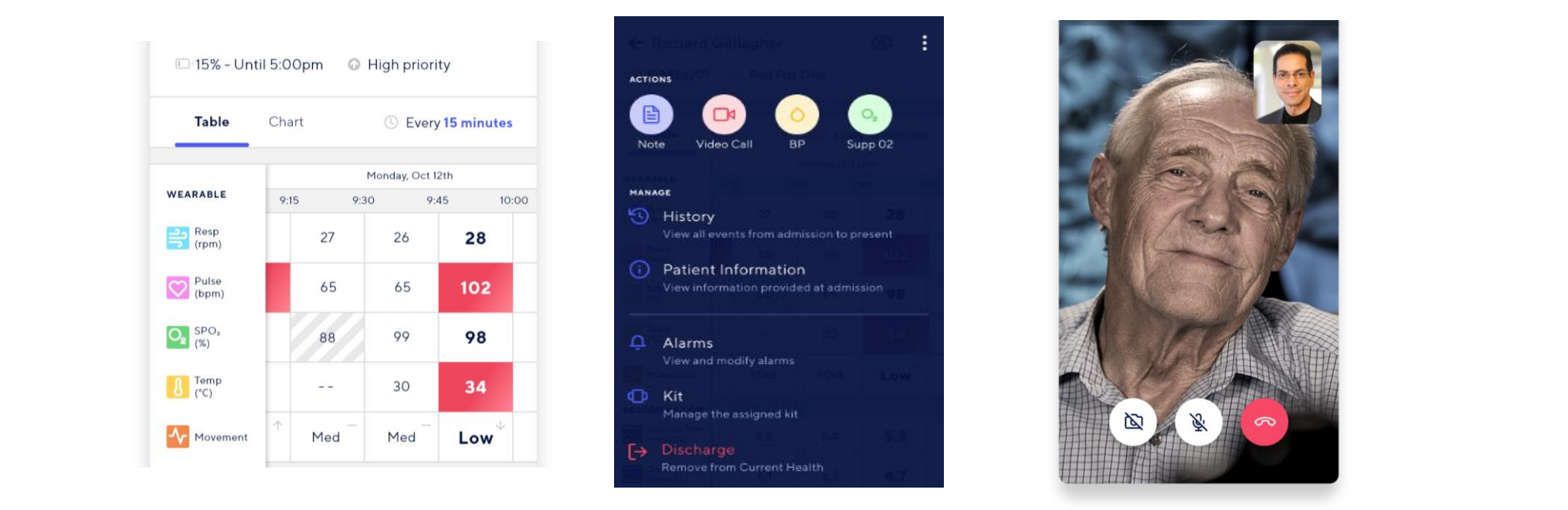
Early on in the study patients may use first-generation devices prior to the study transitioning to the second-generation device (far left); internal components are also shown (near left).

Figure 3. Patient Interface / View



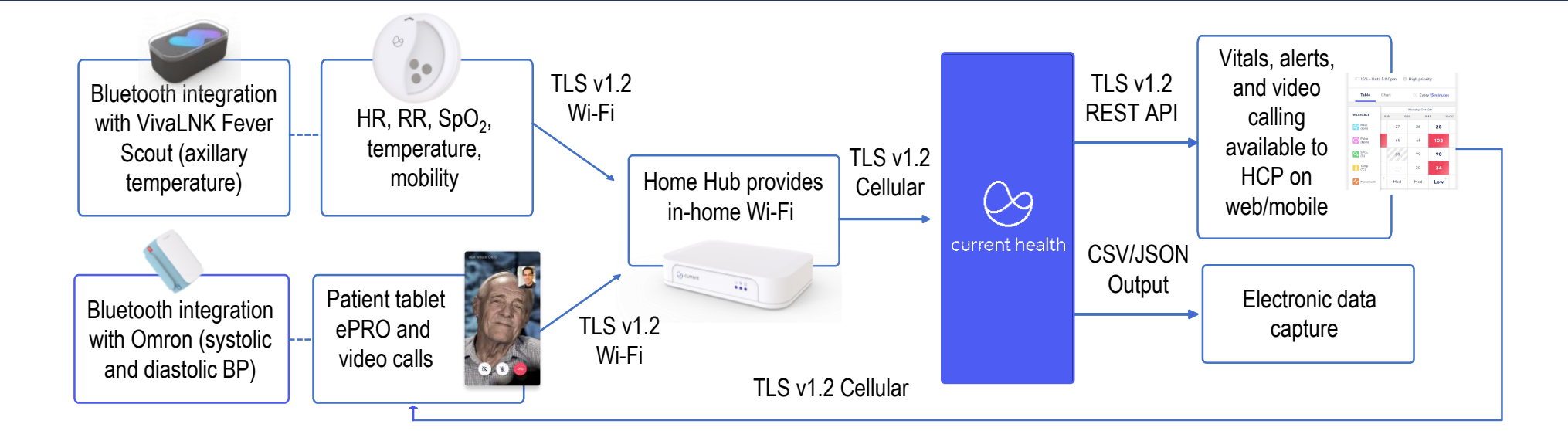
Patients are provided a fully-loaded and easy-to-use tablet which provides setup instructions, helps with daily study requirements, and enables on-demand clinical support and assessment via video call and chat (in English or Spanish).

Figure 4. HCP Interface / View



HCP interface on mobile device and video call are shown; vital sign numbers are displayed in real time.

Figure 5. Transmission of Encrypted Data Over Wi-Fi



Patient vital sign and ePRO data flow through the Current Health platform through the home hub's cellular network. HCPs access vital signs and alerts through mobile or web dashboards through which they can initiate a video call with the patient.

SK, MB-N, KOD, CO, None; SM: Amgen: speaker, advisory boards; DF, Pfizer, Jazz Pharmaceuticals: research funding; MK: Agios: advisory board; JSM, CRISPR: research funding to institution; KG: advisory boards; BioMarin, BMS, Novartis, Blueprint Medicines, TR: Amgen: research funding, consultancy, membership on an entity's Board of Directors or advisory committees; Jazz Pharmaceuticals: consultancy, membership on an entity's Board of Directors or advisory committees, speakers bureau; Kite: consultancy, membership on an entity's Board of Directors or advisory committees, speakers bureau; AS: Amgen: consultancy, speakers bureau, Stemline: consultancy, speakers bureau; CM: Current Health Chief Executive Officer; FZ, PG: Amgen employee and stockholder; GZ: Amgen employee and stockholder, multiple patents; TP: Rafael Pharmaceuticals: consultancy; AbbVie: consultancy; Genentech, Inc.: consultancy; BMS: consultancy, honoraria, speakers bureau; Karyopharm: research funding; Rafael: research funding; Celgene: consultancy, honoraria, speakers bureau; Amgen: honoraria, speakers bureau; Pharmacodics: speakers bureau.

Table 3. Objectives and Endpoints

Objectives

- **Primary:** To determine the safety of outpatient blinatumomab for complete 28-day c1V cycles during monitoring period
- **Key secondary:**
 - To determine the time from first detection of grade 3 or 4 vital sign (per CTCAE v5.0) or significant clinical change to therapeutic intervention during the monitoring period
 - To evaluate the safety and tolerability of blinatumomab administered outpatient

Endpoints

- Primary: Incidence of grade 3 and/or 4 CRS, NT, or any AE requiring hospitalization during the monitoring period
- Key secondary:
 - Time from first onset of fever, hypotension, hypoxia, other grade 3 or 4 vital sign or adverse event including seizure or neurological change (grade 3 limiting self-care activities of daily living) to therapeutic intervention
 - Overall incidence and severity of treatment-emergent AEs and AEs of interest, in particular CRS and NT

AE, adverse event; CRS, cytokine release syndrome; NT, neurotoxicity; therapeutic intervention, measurable action taken by or performed on the patient due to onset of the clinical parameters, actions may include HCP advice to dial 911 / emergency medical services, discontinuation of blinatumomab, taking/receiving a medication/intervention by any medical services, eg, IV fluids or oxygen.

Figure 6. Vital Sign and Clinical Monitoring

Education	Monitoring	Intervention
- HCP, patient, and caregiver will be trained in the use of Current Health monitoring devices (upper arm, temperature, BP, tablet) - Patient will wear devices to establish baseline vital signs, comfort, and eligibility - Patient/caregiver trained to recognize clinical symptoms such as increased lethargy, mental status changes, seizure, jitteriness, fever, fast or difficult breathing, etc. - Patient/caregiver educated - On usual blinatumomab infusion side effects - To contact HCP for any change / new finding - HCP trained on outpatient blinatumomab infusion and response per monitoring described in central panel	- Establish screening baseline values - Remote monitoring vital signs (VS) - Continuous: heart rate (HR), temperature (T), oxygen saturation (SpO₂) - Intermittent: respiratory rate (RR) every 30 seconds, blood pressure (BP) every 3-6 hours, more frequent as per HCP - Alert if ≥ 10 minutes of - HR ≤60 or ≥150 - RR ≤10 or ≥25 - Systolic BP ≤100 mmHg or ≥20% reduction from baseline - T ≥38°C (=axillary ≥37°C) - SpO₂ ≤92% - Neurological symptoms for intervention - Any seizure - Aphasia (receptive or expressive) - Apraxia - Altered level of consciousness - Impairment of cognitive skills - Motor weakness - Change of grade ≥3 self-care activities of daily living - Any change identified by patient or caregiver	- Patient stays within an hour's drive of advanced medical center - Pre-dose dexamethasone (20 mg) given prior to blinatumomab every cycle - Oral doses of corticosteroid available at home to be taken under HCP direction - Cycle 1, day 1: Patient to remain at infusion center for <u>5</u> hours after starting blinatumomab - Cycle 2, day 1: Patient to remain at infusion center for <u>2</u> hours after starting blinatumomab - Cycles 3/4: HCP to follow prescribing information regarding patient monitoring - Immediate alert to HCP if - Abnormal VS for ≥10 minutes - Change in clinical status per patient/caregiver - No data transfer for 15 minutes - HCP will contact/communicate with patient/caregiver via phone/tablet video - HCP response per monitoring described in central panel - HCP may contact patient/caregiver for any concerns (even in the absence of an alert) - Patient/caregiver may contact HCP or emergency services directly as needed

- CHWMS (Figures 2–5) is an FDA-cleared platform for wireless and wearable health monitoring of patients at home, in skilled nursing facilities, or in hospitals, with both audible and visual physiologic multi-parameter alarms.
- Infusion pump and blinatumomab are provided as per site standard and approved prescribing information.
 - The CHWMS provides continuous HR, RR, and SpO₂; continuous temperature from an axillary temperature sensor integrates with the upper arm device via Bluetooth integration.
 - Upper arm Current Health device: monitors HR, RR, and SpO₂, worn securely and tightly such that it moves with the skin as any air gap can produce false readings or no readings for pulse oximetry.
 - Patients manually measure blood pressure (BP) every 3–6 hours around the clock with an approved and integrated BP monitor applied to the other arm/wrist. Tablet captures systolic and diastolic BP via Bluetooth integration.
 - Considerable patient movement can suppress measurement of vital signs.
 - Patients have an integrated mobile device (tablet) to facilitate audio and video contact with the HCP if needed. Tablet also allows capture of ePROs. HCP/designee has a mobile device (smart phone) and receives vital signs as a constant live feed transmitted from the CHWMS device.
 - HCP may initiate direct audio and visual contact with the patient when alerted by the CHWMS device or in the absence of an alert, including video calls for neurological assessment occurring at least every 12 hours.
 - Patients are required to have a caregiver present during the entire period of outpatient monitoring. Patients have a full set of replacement devices as well. There is a 24/7 hotline for patients, caregivers, and HCPs for device support by phone or instant message via app.

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5. Gökbüget, N, et al. *Leuk Lymphoma*. 2020. 61(11): p. 2665-2673.

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