

Supplemental Table S1. Additional information regarding the administration of brentuximab vedotin

1. Drug name (chemical, generic, and brand name or names)	Brentuximab vedotin is marketed in the US as ADCETRIS™ (brentuximab vedotin) for Injection. ADCETRIS is a CD30-directed antibody-drug conjugate (ADC) consisting of three components: 1) the chimeric IgG1 antibody cAC10, specific for human CD30, 2) the microtubule disrupting agent MMAE, and 3) a protease-cleavable linker that covalently attaches MMAE to cAC10. Approximately 4 molecules of MMAE are attached to each antibody molecule.
2. Dose (along with any modifications made for BMI, hematologic parameters, renal function, or other factors)	The recommended dose is 1.8 mg/kg administered only as an intravenous infusion over 30 minutes every 3 weeks. <u>Patients with a weight of >100 kg:</u> The dose for patients with a weight of >100 kg should be calculated for 100 kg. <u>Peripheral neuropathy:</u> Peripheral neuropathy should be managed using a combination of dose delay and reduction to 1.2 mg/kg. For new or worsening Grade 2 or 3 neuropathy, dosing should be held until neuropathy improves to Grade 1 or baseline and then restarted at 1.2 mg/kg. For Grade 4 peripheral neuropathy, ADCETRIS should be discontinued. <u>Neutropenia:</u> Neutropenia should be managed by dose delays and reductions. The dose of ADCETRIS should be held for Grade 3 or 4 neutropenia until resolution to baseline or Grade 2 or lower. Growth factor support should be considered for subsequent cycles in patients who experience Grade 3 or 4 neutropenia. In patients with recurrent Grade 4 neutropenia despite the use of growth factors, discontinuation or dose reduction of ADCETRIS to 1.2 mg/kg may be considered.
3. Route (if parenteral, is central venous access required?)	ADCETRIS is administered only as an intravenous infusion over 30 minutes. Do not administer as an intravenous push or bolus.
4. Type and volume of diluent for if drug is not given IV push direct from vial; rate of administration	ADCETRIS (brentuximab vedotin) for Injection is supplied as single-use vials that contain 50 mg of brentuximab vedotin. <u>Reconstitution:</u> Following reconstitution with 10.5 mL Sterile Water for Injection, USP, a solution containing 5 mg/mL brentuximab vedotin is produced. <u>Dilution:</u> Immediately add the reconstituted solution to an infusion bag containing a minimum volume of 100 mL to achieve a final concentration of 0.4 mg/mL to 1.8 mg/mL brentuximab vedotin. ADCETRIS can be diluted into 0.9% Sodium Chloride Injection, 5% Dextrose Injection or Lactated Ringer's Injection. Do not mix ADCETRIS with, or administer as an infusion with, other medicinal products. <u>Rate of administration:</u> ADCETRIS is administered only as an intravenous infusion over 30 minutes.
5. Cycle length and number of cycles, or criteria for discontinuation	ADCETRIS is administered every 3 weeks. Continue treatment until a maximum of 16 cycles, disease progression or unacceptable toxicity.
6. Premedications and concurrent medications (including hydration, anti-emetics, growth factors, or any other relevant supportive medications)	<u>Infusion reactions:</u> Infusion-related reactions, including anaphylaxis, have occurred with ADCETRIS. Monitor patients during infusion. If anaphylaxis occurs, immediately and permanently discontinue administration of ADCETRIS. Patients who have experienced a prior infusion-related reaction should be premedicated for subsequent infusions. Premedication may include acetaminophen, an antihistamine and a corticosteroid. <u>Drug interactions:</u> In vitro data indicate that monomethyl auristatin E (MMAE) is a substrate and an inhibitor of CYP3A4/5. Patients who are receiving strong CYP3A4 inhibitors concomitantly with ADCETRIS should be closely monitored for adverse reactions. ADCETRIS is not expected to alter the exposure to drugs that are metabolized by CYP3A4 enzymes.
7. Patient monitoring parameters (frequency of visits and blood draws during therapy)	Complete blood counts should be monitored prior to each dose of ADCETRIS and more frequent monitoring should be considered for patients with Grade 3 or 4 neutropenia.

Source: Full prescribing information for ADCETRIS™ (brentuximab vedotin) for Injection, January 2012.

Supplemental Table S2. Patients with CMV viremia post brentuximab vedotin

Patient (sex/age)	AlloSCT	Interval between alloSCT and brentuximab vedotin			CMV viremia post brentuximab vedotin
		Duration	GVHD?	CMV history*	
1 (F/39)	Patient in remission prior to alloSCT. Flu/CY/TBI conditioning. Unrelated donor (match status unknown). AlloSCT resulted in CR.	4.9 years	No evidence of GVHD	Unknown serology status; no evidence of viremia or infection	Received 9 cycles of brentuximab vedotin. Positive PCR at initial test and intermittently viremic for 6 months while on study (range 44-920 copies/mL). Received antiviral therapy and remained asymptomatic without evidence of CMV dissemination.
2 (F/26)	Patient disease status prior to alloSCT unknown. Flu/busulfan/TLI conditioning. Donor type MRD. AlloSCT resulted in CR.	6.0 years	Acute GVHD	Unknown serology status and history of viremia or infection	Received 1 cycle of brentuximab vedotin. Developed <i>Streptococcus pneumoniae</i> sepsis and pneumonia on study day 2. BAL fluid was negative for CMV by DFA and shell vial but positive by culture. Developed multisystem organ failure as a result of unremitting sepsis. Despite treatment with ganciclovir, the patient died on study day 21. Retrospective, centralized testing for CMV was positive beginning on study day 1 (60 copies/mL; subsequently 460-670 copies/mL), consistent with local PCR results, which revealed a rising number of copies that rapidly decreased after initiation of ganciclovir treatment.
3 (M/25)	Patient had relapsed/refractory disease prior to alloSCT. ChlVPP conditioning. Donor type MUD. AlloSCT resulted in CR.	3.9 years	No evidence of GVHD	Positive serology status; no evidence of viremia or infection	Received 6 cycles of brentuximab vedotin. Retrospective testing for CMV viremia by PCR was negative at baseline but intermittently positive at low levels through cycles 1 and 2 of treatment (range 95-130 copies/mL). No antiviral therapy was given and there was no evidence of dissemination of CMV.
4 (M/41)	Patient in remission prior to alloSCT. Flu/melphalan/ICE/ alemtuzumab conditioning. Donor type MUD. AlloSCT resulted in CR.	6.3 years	Chronic GVHD	Positive serology status; history of clinical infection	Received 6 cycles of brentuximab vedotin. Persistently negative testing for CMV by PCR until EOT (85 copies/mL). At time of EOT the patient developed multi-drug resistant pseudomonas pneumonia, empyema, sepsis, and renal failure. Supportive care was withdrawn and the patient died. No additional testing for CMV was performed, and not antiviral therapy was given.
5 (F/27)	Patient had relapsed/refractory disease prior to alloSCT. Flu/CY conditioning. Donor type MMUD. AlloSCT resulted in CR.	1.3 years	Acute GVHD	Positive serology status; history of viremia	Received 1 cycle of brentuximab vedotin. Prior to the initiation of study-related CMV testing, routine local surveillance revealed CMV viremia (range 633-1070 copies/mL) that was successfully treated with antiviral therapy. The patient remained asymptomatic and no evidence of dissemination was reported.

BAL indicates bronchoalveolar lavage; ChlVPP, chlorambucil/vinblastine/procarbazine/prednisolone; CR, complete remission; CY, cyclophosphamide; DFA, direct fluorescent antibody; EOT, end of treatment visit; Flu, fludarabine; GVHD, graft-versus-host disease; MMUD, mismatched unrelated donor; MRD, matched related donor; MUD, matched unrelated donor; PCR, polymerase chain reaction.

* Viremia is defined as evidence that CMV is active and replicating but has not caused an invasive infection.