

Form 4100 R6.0: Cellular Therapy Essential Data Follow-Up Form

Center: _____

CRID: _____

Key Fields

Sequence Number: _____

Date Received: ____-____-____

CIBMTR Center Number: _____

CIBMTR Research ID: _____

Event date: ____-____-____

Visit

100 day 6 months 1 year 2 years > 2 years,

Specify: _____

Product

Questions: 1 - 1

1 Name of cellular therapy product (for most recent cell therapy infusion)

- Axicabtagene ciloleucel (Yescarta®)
- Brexucabtagene autoleucel (Tecartus™)
- Ciltacabtagene autoleucel (JNJ-4528)
- Idecabtagene vicleucel
- Letetresgene autoleucel
- Lisocabtagene maraleucel (Breyanzi™)
- Orvacabtagene autoleucel
- Tisagenlecleucel (Kymriah®)
- Other product
- No product name

Survival

Questions: 2 - 3

2 Date of actual contact with the recipient to determine medical status for this follow-up report: ____-____-____

3 Specify the recipient's survival status at the date of last contact

- Alive - Answers to subsequent questions should reflect clinical status since the date of last report
- Dead - Answers to subsequent questions should reflect clinical status between the date of last report and immediately prior to death. Complete a Form 2900 - Recipient Death Data.

Subsequent Cellular Infusions

Questions: 4 - 8

All additional cellular therapy infusions given for the same indication per protocol require a separate infusion form and should be reported on the Form 4000 for this course of cellular therapy. If a cellular therapy was administered for treatment of a different indication, or in response to disease progression / no response, a new Form 4000 (Pre-CTED) must be completed.

4 Has the recipient received a new course of cellular therapy (unplanned) since the date of last report?

- Yes No

5 Specify the reason for which cellular therapy was given

- Failure to respond or in response to disease assessment
- New indication

6 Date of cellular therapy: ____-____-____ Also complete a Cellular Therapy Essential Data Pre-Infusion Form 4000

7 Did the recipient receive an HCT since the date of last report?

- Yes - Also complete a Pre-TED Form 2400 for the subsequent HCT
- No

8 Date of HCT: ____-____-____

Best Response to Cellular Therapy

Questions: 9 - 11

9 What was the best response to the cellular therapy?

- Continued complete response (CCR) (for recipients in CR at the time of cellular therapy infusion)
- Complete response
- Normalization of organ function
- Partial response
- Partial normalization of organ function
- No response
- Disease progression or worsening of organ function

10 Was the date of best response previously reported?

- yes no

11 Date response established: ____-____-____

Peripheral Blood Count Recovery

Questions: 12 - 20

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12 Was there evidence of initial recovery?

- Yes (ANC $\geq 500/mm^3$ achieved and sustained for 3 lab values)
 No (ANC $\geq 500/mm^3$ was not achieved)
 Not applicable (ANC never dropped below $500/mm^3$ at any time after the start of lymphodepleting therapy / no lymphodepleting therapy given)
 Previously reported (recipient's initial recovery was recorded on a previous report)

13 Date ANC $\geq 500/mm^3$ (first of 3 consecutive lab values) _____ - _____ - _____

14 Following the initial recovery, was there subsequent decline in ANC to $< 500/mm^3$ for ≥ 3 days since the date of last report?

- yes no

15 Date of decline in ANC to $< 500/mm^3$ for ≥ 3 days: (first of 3 days that the ANC declined) _____ - _____ - _____

16 Did recipient recover and maintain ANC $\geq 500/mm^3$ following the decline?

- yes no

17 Date of ANC recovery

- Known Unknown

18 Date of ANC recovery: _____ - _____ - _____

19 Was an initial platelet count $\geq 20 \times 10^9/L$ achieved?

- Yes
 No
 Not applicable (platelet count never dropped below $20 \times 10^9/L$ at any time after the start of lymphodepleting therapy / no lymphodepleting therapy given)
 Previously reported ($\geq 20 \times 10^9/L$ was achieved and reported previously)

20 Date platelets $\geq 20 \times 10^9/L$: _____ - _____ - _____

Disease Relapse or Progression

Questions: 21 - 22

21 Was a disease relapse or progression detected since the date of last report?

- yes no

22 Date of relapse or progression: _____ - _____ - _____

Current Hematologic Findings

Questions: 23 - 33

23 Date of most recent complete blood count (CBC) sample drawn: _____ - _____ - _____

24 Complete blood count results available (check all that apply)

- WBC
 Neutrophils
 Lymphocytes
 Hemoglobin
 Hematocrit
 Platelets

25 WBC: _____ $\times 10^9/L$ ($\times 10^3/mm^3$)
 $\times 10^6/L$

26 Neutrophils: _____ %

27 Lymphocytes: _____ %

28 Hemoglobin: _____ g/dL g/L mmol/L

29 Hematocrit: _____ %

30 Were RBCs transfused ≤ 30 days before the date the sample was drawn?

- Yes No

31 Platelets: _____ $\times 10^9/L$ ($\times 10^3/mm^3$)
 $\times 10^6/L$

32 Were platelets transfused ≤ 7 days before the date the sample was drawn?

- Yes No

33 Did the recipient receive any growth factors ≤ 7 days before the date the sample was drawn?

- Yes No

New Malignancy, Lymphoproliferative or Myeloproliferative Disease / Disorder

Questions: 34 - 34

Report new malignancies that are different than the indicated disease / disorder for which this cellular therapy was performed. Do NOT include relapse, progression or transformation of the same disease subtype.

34 Did a new malignancy, myelodysplastic, myeloproliferative, or lymphoproliferative disease / disorder occur that is different from the disease / disorder for which the infusion was performed? (include clonal cytogenetic abnormalities, and post-transplant lymphoproliferative disorders)

- Yes - Also complete Subsequent Neoplasms Form 3500
 No
 Previously reported (form 3500 has already been submitted for this event)

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Persistence of Cells

Questions: 35 - 59

This section pertains to the evaluation of persistence of a cellular product in the recipient.

35 Were tests performed to detect persistence of the cellular product since the date of last report?

Yes No

36 Was persistence evaluated by molecular assay? (e.g. PCR)

Yes No

37 Date sample collected: ____ - ____ - ____

38 Specify the cell source (check all that apply)

- Bone marrow
- Peripheral blood
- Tumor
- Other source

39 Specify other cell source: _____

40 Were the infused cells detected?

Yes No

41 Was persistence evaluated by flow cytometry testing? (immunophenotyping)

Yes No

42 Date sample collected: ____ - ____ - ____

43 Specify the cell source (check all that apply)

- Bone marrow
- Peripheral blood
- Tumor
- Other source

44 Specify other cell source: _____

45 Were the infused cells detected?

Yes No

46 Were B-cell counts monitored after infusion?

Yes No

47 Was there B-cell recovery?

Yes No

48 Date of B-cell recovery: ____ - ____ - ____

49 Was persistence evaluated by immunohistochemistry?

Yes No

50 Date sample collected: ____ - ____ - ____

51 Specify the cell source (check all that apply)

- Bone marrow
- Peripheral blood
- Tumor
- Other source

52 Specify other cell source: _____

53 Were the infused cells detected?

Yes No

54 Was persistence evaluated by another method?

Yes No

55 Specify other method: _____

56 Date sample collected: ____ - ____ - ____

57 Specify the cell source (check all that apply)

- Bone marrow
- Peripheral blood
- Tumor
- Other source

58 Specify other cell source: _____

59 Were the infused cells detected?

Yes No

Graft vs. Host Disease

Questions: 60 - 79

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This section is for allogeneic infusions only. If this was an autologous infusion, continue to the "Toxicities" section.

60 Did acute GVHD develop since the date of last report?

- Yes No Unknown

61 Date of acute GVHD diagnosis: ____ - ____ - ____

62 Did acute GVHD persist since the date of last report?

- Yes No Unknown

63 Overall grade of acute GVHD at diagnosis

- I - Rash on \leq 50% of skin, no liver or gut involvement
 II - Rash on $>$ 50% of skin, bilirubin 2-3 mg/dL, or diarrhea 500-1000 mL/day or persistent nausea or vomiting
 III - Bilirubin 3-15 mg/dL, or gut stage 2-4, diarrhea $>$ 1000 mL/day or severe abdominal pain with or without ileus
 IV - Generalized erythroderma with bullous formation, or bilirubin $>$ 15 mg/dL
 Not applicable (acute GVHD present but grade is not applicable)

List the stage for each organ at diagnosis of acute GVHD:

64 Skin

- Stage 0 - No rash, no rash attributable to acute GVHD
 Stage 1 - Maculopapular rash, $<$ 25% of body surface
 Stage 2 - Maculopapular rash, 25-50% of body surface
 Stage 3 - Generalized erythroderma, $>$ 50% of body surface
 Stage 4 - Generalized erythroderma with bullae formation and/or desquamation

65 Lower intestinal tract (*use mL/day for adult recipients and mL/kg/day for pediatric recipients*)

- Stage 0 - No diarrhea, no diarrhea attributable to acute GVHD / diarrhea $<$ 500 mL/day (adult), or $<$ 10 mL/kg/day (pediatric)
 Stage 1 - Diarrhea 500-1000 mL/day (adult), or 10-19.9 mL/kg/day (pediatric)
 Stage 2 - Diarrhea 1001-1500 mL/day (adult), or 20-30 mL/kg/day (pediatric)
 Stage 3 - Diarrhea $>$ 1500 mL/day (adult), or $>$ 30 mL/kg/day (pediatric)
 Stage 4 - Severe abdominal pain, with or without ileus, and/or grossly bloody stool

66 Upper intestinal tract

- Stage 0 - No persistent nausea or vomiting
 Stage 1 - Persistent nausea or vomiting

67 Liver

- Stage 0 - No liver acute GVHD / bilirubin $<$ 2.0 mg/dL ($<$ 34 μ mol/L)
 Stage 1 - Bilirubin 2.0-3.0 mg/dL (34-52 μ mol/L)
 Stage 2 - Bilirubin 3.1-6.0 mg/dL (53-103 μ mol/L)
 Stage 3 - Bilirubin 6.1-15.0 mg/dL (104-256 μ mol/L)
 Stage 4 - Bilirubin $>$ 15.0 mg/dL ($>$ 256 μ mol/L)

68 Other site(s) involved with acute GVHD

- Yes No

69 Specify other site(s): _____

Specify the MAXIMUM overall grade of acute GVHD since the date of last report:

70 Maximum overall grade of acute GVHD

- I - Rash on \leq 50% of skin, no liver or gut involvement
 II - Rash on $>$ 50% of skin, bilirubin 2-3 mg/dL, or diarrhea 500-1000 mL/day or persistent nausea or vomiting
 III - Bilirubin 3-15 mg/dL, or gut stage 2-4 diarrhea $>$ 1000 mL/day or severe abdominal pain with or without ileus
 IV - Generalized erythroderma with bullous formation, or bilirubin $>$ 15 mg/dL
 Not applicable (acute GVHD present but grade is not applicable)

71 Date maximum overall grade of acute GVHD: ____ - ____ - ____

72 Did chronic GVHD develop since the date of last report?

- Yes No Unknown

73 Date of chronic GVHD diagnosis: ____ - ____ - ____ Date estimated

74 Did chronic GVHD persist since the date of last report?

- Yes No Unknown

Specify the MAXIMUM grade of chronic GVHD since the date of last report:

75 Maximum grade of chronic GVHD (*according to best clinical judgment*)

- Mild Moderate Severe Unknown

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76 Specify if chronic GVHD was limited or extensive

- Limited - Localized skin involvement and/or liver dysfunction
- Extensive - One or more of the following:
- Generalized skin involvement; or,
 - Liver histology showing chronic aggressive hepatitis, bridging necrosis or cirrhosis; or,
 - Involvement of eye: Schirmer's test with < 5 mm wetting; or
 - Involvement of minor salivary glands or oral mucosa demonstrated on labial biopsy; or
 - Involvement of any other target organ

77 Date of maximum grade of chronic GVHD: ____ - ____ - ____

78 Is the recipient still taking systemic steroids? (Do not report steroids for adrenal insufficiency, ≤ 10 mg/day for adults, < 0.1 mg/kg/day for children)

- Yes No Not Applicable Unknown

79 Is the recipient still taking (non-steroid) immunosuppressive agents (including PUVA) for GVHD?

- Yes No Not Applicable Unknown

Toxicities

Questions: 80 - 170

Cytokine Release Syndrome (CRS)

80 Did the recipient experience Cytokine Release Syndrome (CRS)?

- Yes No

81 Was the date of diagnosis previously reported?

- Yes No

82 Date of CRS diagnosis: ____ - ____ - ____

83 Specify therapy given for CRS (check all that apply)

- Anakinra
- Corticosteroids
- Siltuximab
- Tocilizumab
- Other therapy
- No therapy given

84 Specify other therapy: _____

85 Doses of tocilizumab given

- 1 ≥ 2

86 Indicate the symptoms of CRS (check all that apply)

- Fevers (> 100.4 F or > 38 C)
- Hypotension requiring therapy
- Hypoxia requiring minimal supplemental oxygen (FiO2 < 40%)
- Hypoxia requiring more than minimal supplemental oxygen (FiO2 ≥ 40%)
- Unknown

87 Date of fever onset: ____ - ____ - ____

88 Date of hypotension onset: ____ - ____ - ____

89 Specify therapy given for hypotension (check all that apply)

- Intravenous fluids
- Vasopressor(s)
- Other

90 Specify other therapy: _____

91 Specify the number of vasopressors used for therapy

- 1 ≥2

92 Specify the vasopressor(s) used (check all that apply)

- Phenylephrine
- Norepinephrine
- Epinephrine
- Dopamine
- Vasopressin
- Other

93 Specify other vasopressor: _____

94 Was hypotension controlled with therapy?

- Yes No Unknown

95 Date of hypoxia onset for minimal supplemental oxygen: (FiO2 < 40%) ____ - ____ - ____

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96 Date of hypoxia onset for more than minimal supplemental oxygen: ($FI_{O_2} \geq 40\%$) _____ - _____ - _____

97 Was positive pressure ventilatory support required? (CPAP, BiPAP, intubation and mechanical ventilation)

- Yes No Unknown

98 Date started: _____ - _____ - _____

99 Were there features related to macrophage activation syndrome (MAS) / hemophagocytic lymphohistiocytosis (HLH)?

- Yes No

100 Date of MAS / HLH onset: _____ - _____ - _____

101 Did the recipient have splenomegaly?

- yes no

102 Was MAS / HLH confirmed by a bone marrow biopsy?

- Yes No

103 Specify the laboratory values collected (check all that apply)

- Fibrinogen
 Triglyceride
 None

104 Lowest fibrinogen level: _____ mg/dL mg/L

105 Date fibrinogen sample collected: _____ - _____ - _____

106 Highest triglyceride level: _____ mg/dL mmol/L

107 Date triglyceride sample collected: _____ - _____ - _____

108 Did cytokine release syndrome resolve?

- Yes No

109 Date resolved: _____ - _____ - _____

Neurotoxicity (ICANS)

110 Did the recipient experience neurotoxicity (ICANS)?

- Yes No

111 Was the date of onset previously reported?

- Yes No

112 Date of neurotoxicity (ICANS) onset: _____ - _____ - _____

113 Specify therapy given for neurotoxicity (check all that apply)

- Anti-epileptics
 Anakinra
 Corticosteroids
 Siltuximab
 Tocilizumab
 Other therapy
 No therapy given

114 Specify other therapy: _____

115 Which cognitive assessment was performed?

- CARTOX ICE None

116 What was the lowest score?

- 10
 9
 8
 7
 6
 5
 4
 3
 2
 1
 0
 Unable to complete assessment

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For symptoms of neurotoxicity (ICANS), report the HIGHEST grade observed in this reporting period

117 Indicate the symptoms of neurotoxicity (ICANS) (check all that apply)

- Aphasia (speech impairment resulting in full loss of language)
- Cerebral edema
- Cerebrovascular accident (stroke)
- Depressed level of consciousness
- Dysphasia (speech impairment resulting in partial loss of language)
- Hallucinations
- Hemiparesis / paraparesis / other motor deficit
- Leukoencephalopathy
- Seizure
- Tremors
- Other symptom

118 Specify other symptom: _____

119 Specify type of cerebral edema

- Focal / local edema on neuroimaging
- Diffuse cerebral edema on neuroimaging; decerebrate or decorticate posturing; or cranial nerve VI palsy; or papilledema; or Cushing's triad

120 Date of cerebrovascular accident onset: ____ - ____ - ____

121 Specify type of cerebrovascular accident

- Hemorrhagic
- Ischemic

122 Specify the most severe level of depressed level of consciousness

- Awakens spontaneously
- Awakens to voice
- Awakens only to tactile stimulus
- Patient unarousable or requires vigorous or repetitive tactile stimuli to arouse; stupor or coma

123 Specify the grade of dysphasia

- 1 (awareness of receptive or expressive characteristics; not impairing ability to communicate)
- 2 (moderate receptive or expressive characteristics; impairing ability to communicate spontaneously)

124 Specify the type of seizure

- Complex partial
- Generalized tonic-clonic
- Non-convulsive status epilepticus
- Simple partial
- Status epilepticus
- Other type
- Unknown

125 Specify other type: _____

126 Specify the severity of the seizure

- Grade 3 (any clinical seizure focal or generalized that resolves rapidly; or non-convulsive seizures on EEG that resolve with intervention)
- Grade 4 (life-threatening prolonged seizure that is > 5 min; or repetitive clinical or electrical seizures without return to baseline in between)

127 Did neurotoxicity (ICANS) resolve?

- Yes
- No

128 Date resolved: ____ - ____ - ____

Other toxicities

129 Hypogammaglobulinemia

- Yes
- No
- Unknown

130 Was the date of onset previously reported?

- Yes
- No

131 Date of onset: ____ - ____ - ____

132 Did hypogammaglobulinemia resolve?

- Yes
- No

133 Date resolved: ____ - ____ - ____

134 Did recipient require immunoglobulin replacement therapy?

- Yes
- No

135 Is the recipient still requiring replacement therapy?

- Yes
- No

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136 Tumor lysis syndrome

Yes No Unknown

137 Was the date of onset previously reported?

Yes No

138 Date of onset: ____ - ____ - ____

139 Grade

3 4 5

140 Did tumor lysis syndrome resolve?

Yes No

141 Date resolved: ____ - ____ - ____

142 Other toxicity

Yes No Unknown

Other Toxicities (1)

Questions: 143 - 147

143 Specify other toxicity: _____

144 Was the date of onset previously reported?

Yes No

145 Date of onset: ____ - ____ - ____

146 Did other toxicity resolve?

Yes No

147 Date resolved: ____ - ____ - ____

Specify if the recipient has experienced any of the following since the date of last report:

148 Has the recipient experienced a grade 3 organ toxicity?

Yes No Unknown

Grade 3 Toxicities (1)

Questions: 149 - 154

149 Specify organ

Cardiovascular Gastrointestinal Kidneys Liver Lungs Musculoskeletal Nervous system Other

150 Specify the toxicity _____

151 Was the date of onset previously reported?

Yes No

152 Date of onset: ____ - ____ - ____

153 Did the grade 3 toxicity resolve?

Yes No

154 Date resolved ____ - ____ - ____

155 Has the recipient experienced a grade 4 organ toxicity?

Yes No Unknown

Grade 4 Toxicities (1)

Questions: 156 - 161

156 Specify organ

Cardiovascular Gastrointestinal Kidneys Liver Lungs Musculoskeletal Nervous system Other

157 Specify the toxicity _____

158 Was the date of onset previously reported?

Yes No

159 Date of onset: ____ - ____ - ____

160 Did the grade 4 toxicity resolve?

Yes No

161 Date resolved: ____ - ____ - ____

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162 Specify the laboratory values collected (*check all that apply*)

- C-reactive protein
- Interleukin-6
- Soluble interleukin-2 receptor α (*sIL2RA or soluble CD25*)
- Total serum ferritin
- None

Specify the **MAXIMUM** lab results since the date of last report:

163 Maximum C-reactive protein: _____ mg/dL mg/L

164 Date C-reactive protein collected: _____ - _____ - _____

165 Maximum interleukin-6: _____ pg/mL IU/mL

166 Date Interleukin-6 collected: _____ - _____ - _____

167 Maximum soluble interleukin-2 receptor α : _____ pg/mL IU/mL U/mL

168 Date soluble interleukin-2 receptor α collected: _____ - _____ - _____

169 Maximum total serum ferritin: _____ ng/mL (μ g/L)

170 Date serum ferritin collected: _____ - _____ - _____

Infection

Questions: 171 - 175

171 Did the recipient develop a clinically significant infection since the date of last report?

- Yes No

Infection (1)

Questions: 172 - 175

Report each infection organism, site, and date of diagnosis

172 Organism _____

173 Specify other organism: _____

174 Site (*check all that apply*)

- Blood
- Bone
- CNS
- Eyes
- Genital area
- GI tract, Lower
- GI tract, Upper
- Joints
- Liver/Spleen
- Lung
- Sinus and/or Upper respiratory tract
- Skin, cellulitis
- Skin, necrotizing fasciitis
- Urinary tract, Lower
- Urinary tract, Upper

175 Date of diagnosis: _____ - _____ - _____

Pregnancy Status

Questions: 176 - 177

176 Was the recipient pregnant at any time in this reporting period? (**Female only**)

- Yes - **Also complete Pregnancy Form 3501**
- No
- Unknown
- Previously reported (*form 3501 already submitted for this event*)

177 Was the recipient's female partner pregnant at any time in this reporting period? (**Male only**)

- Yes - **Also complete Pregnancy Form 3501**
- No
- Unknown
- Previously reported (*form 3501 already submitted for this event*)

First Name: _____

Last Name: _____

E-mail address: _____

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Date: ____ - ____ - ____