### Appendix Table 4a. Hydroxyurea Toxicity in Randomized, Controlled Trials in Diseases Other than Sickle Cell Disease

<table>
<thead>
<tr>
<th>Study, Year (Reference)</th>
<th>Location</th>
<th>Recruitment Period</th>
<th>Inclusion/Exclusion Criteria</th>
<th>Intervention</th>
<th>Starting Dose*</th>
<th>Jadad Score (10)</th>
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</thead>
<tbody>
<tr>
<td>HIV</td>
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</tbody>
</table>
| Frank et al., 2004† (66)| North America | Oct 96–Jan 98 | **Inclusion:** Age >18; HIV positive; ANC >1 x 10^9 cells/L, platelet >75 x 10^9 cells/L; Hb >9.2 g/L for men, >8.8 g/L for women, CD4 count 0.2–0.7 cells x 10^9 cells/L  
**Exclusion:** Preg; renal failure; liver failure; prior HU; pancreatitis; peripheral neuropathy  | HU (low dose) with/without ddl | HU 1000 mg/d | 4 |
|                        |          |                    |                             | HU (high dose) with/without ddl | HU 1500 mg/d |
| Havlir et al., 2001 (67)| North America | Nov 98–Jul 99 | **Inclusion:** Age >12 years; HIV positive; at least 6 mo on IDV, ZDV (or d4T), and 3TC; HIV RNA <200/ml; CD4 count >0.2 cells x 10^9/L, >0.1 cells x 10^9/L before starting IDV  
**Exclusion:** ANC <1.0 x 10^9 cells/L liver failure AST, ALT >3 ULT, documented or suspected hepatitis; prior treatment with HIV protease inhibitor other than IDV or both ddl and d4T; thrombocytopenia <75 cells x 10^9/L; anemia <8.9 for female and 9.1 g/L for men; history of grade 2 or greater peripheral neuropathy  | HU IDV ddl d4T | HU 600 BID | 2 |
|                        |          |                    |                             | IDV ddl d4T + placebo |                |
|                        |          |                    |                             | IDV ZDV(or d4T) 3TC |                |
| Swindells et al., 2005 (68)| North America | Sep 99–Apr 07 | **Inclusion:** Age >12; neutrophil count >1.0 x 10^9 cells/L; HIV-1 RNA 400–100,000 and CD4 count > 0.1 x 10^9 cells/L; failure of initial antiretroviral treatment; not received non-nucleoside reverse transcriptase inhibitors, ABC or ddl; Hb >9 g/L for women >10 g/L for men; plt > 75 x 10^9 cells/L; estimated creatinine clearance >50mL/min, serum lipase <ULN, serum amylase <1.5x ULN, ALT<5x ULN  
**Exclusion:** Preg or breast feeding; acute hepatitis within 6 mo; immunotherapeutic vaccine or cytotoxic agents within 8wks before study start; hx of pancreatitis or peripheral neuropathy within 2m before study start  | ABC/EFV/ddl and HU | HU 500 mg BID | 2 |
<p>|                        |          |                    |                             | ABC/EFV/ddl |                |
| Seminari et al., 1999 (69)| Europe | Jun 05–Jun 05 | <strong>Inclusion:</strong> Hb &gt;10 g/L; normal amylase; neutrophil &gt;1.5 x 10^9 cells/L; included if leukopenia included if plt &gt;150 x 10^9 cells/L; absence of current HIV-associated disease or prior hx of any AIDS-defining illness  | ddl + HU | HU 500 mg BID | 3 |
|                        |          |                    |                             | ddl |                |</p>
<table>
<thead>
<tr>
<th>Study Authors</th>
<th>Location</th>
<th>Dates</th>
<th>Inclusion</th>
<th>Intervention</th>
<th>Exclusion</th>
<th>Notes</th>
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</thead>
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<tr>
<td>Bloch et al., 2006 (70)</td>
<td>Australia</td>
<td>Jan 00–Feb 02</td>
<td><strong>Inclusion:</strong> acute primary HIV infection</td>
<td>Indinavir/ritonavir/ddI + (either stavudine or lamivudine) and HU</td>
<td>HU 500 mg BID</td>
<td>2</td>
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<tr>
<td>Rutschmann et al., 1998 (71)</td>
<td>Europe</td>
<td></td>
<td><strong>Inclusion:</strong> Age ≥ 20 years; HIV positive; CD4 &gt;0.2, &lt;0.5 x 10^9 cells/L (twice); two HIV RNA &gt;1000 cells/mL</td>
<td>ddl/d4T/HU</td>
<td>HU 500 mg bid</td>
<td>3</td>
</tr>
<tr>
<td>Rutschmann et al., 1998 (72)</td>
<td>Europe</td>
<td></td>
<td><strong>Inclusion:</strong> HIV positive; CD4 0.22–0.5 x 10^9 cells/L; HIV RNA &gt;1000/ml; stavudine and HU naive</td>
<td>ddl/stavudine/HU</td>
<td>HU 500 mg BID</td>
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<tr>
<td>Rutschmann et al., 2000 (73)</td>
<td>Europe</td>
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<td><strong>Inclusion:</strong> CD4 0.2–0.5x10^9/L; HIV RNA &gt;1000 x2</td>
<td>ddl/stavudine/HU</td>
<td>HU 500 mg BID</td>
<td>2</td>
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<tr>
<td>Hehlmann et al., 2003 (74)</td>
<td>Europe</td>
<td>Feb 91–Dec 94</td>
<td><strong>Inclusion:</strong> newly diagnosed CML in chronic phase</td>
<td>HU</td>
<td>40 mg/kg/d</td>
<td>2</td>
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<tr>
<td>Benelux CML Study Group, 1998 (75)</td>
<td>Europe</td>
<td>Dec 87–Dec 92</td>
<td><strong>Inclusion:</strong> Age &gt; = 18; previously untreated, newly diagnosed Ph + CML in chronic phase; BCR-ABL (+); WHO performance status 0,1,2; adequate renal/hepatic fnx (bilirubin and creatinine &lt;2x ULN)</td>
<td>IFN-alpha 2a + HU</td>
<td>IFN 5*10^7IU/m2/d + HU added as required</td>
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<tr>
<td>Hehlmann et al., 1994 (76)</td>
<td>Europe</td>
<td>Jul 83–Jan 91</td>
<td><strong>Inclusion:</strong> newly dx-ed. not pretreated CML in chronic phase; fatigue or weight loss or fever or organomegaly related symptoms or WBC &gt;50 x10^9 cells/L or Thrombocytosis &gt;1 million</td>
<td>HU</td>
<td>40 mg/kg/d</td>
<td>3</td>
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<tr>
<td>Broustet et al., 1991 (77)</td>
<td>Europe</td>
<td>May 87 Jul 90</td>
<td><strong>Inclusion:</strong> Age &gt;18; Ph + CML</td>
<td>HU</td>
<td>4 million units/m²</td>
<td>3</td>
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<tr>
<td>Study</td>
<td>Country</td>
<td>Dates</td>
<td>Inclusion</td>
<td>Treatment</td>
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<td>---------------------------------------------------------------------------</td>
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<tr>
<td>Hehlmann et al., 1993 (78)</td>
<td>Europe</td>
<td>Jul 83–Jan 91</td>
<td><strong>Inclusion:</strong> newly diagnosed CML in chronic phase&lt;br&gt;<strong>Exclusion:</strong> not in chronic phase; no treatment required; prior treatment with IFN or irradiation or cytostatics; lack of consent; second neoplasia; any other reason that made treatment with protocol unlikely</td>
<td>HU 40 mg/kg/d&lt;br&gt;Busulfan 0.1 mg/kg/d</td>
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<tr>
<td>Stephens et al., 1984 (79)</td>
<td>North America</td>
<td></td>
<td><strong>Inclusion:</strong> advanced prostate cancer (stage D disease)&lt;br&gt;<strong>Exclusion:</strong> unstable ischemic or rheumatic heart disease; heart failure</td>
<td>HU 3600 mg/m², 2 days/week&lt;br&gt;Adriamycin + cyclophosphamide&lt;br&gt;Adriamycin at 40 mg/m² and cyclophosphamide at 200 mg/m², reduced to AC 20 + cyclophosphamide 100 if in poor–risk group</td>
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<tr>
<td>Loening et al., 1981 (80)</td>
<td>North America</td>
<td>May 77–Apr 79</td>
<td><strong>Inclusion:</strong> histologically proven prostate CA with distant mets and progression</td>
<td>HU 3 g/m²&lt;br&gt;Cyclophosphamide 1 g/m²&lt;br&gt;Methyl-CCNU 175 mg/m²</td>
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<tr>
<td>Najean Cluster/PV</td>
<td>Europe</td>
<td>Jun 05–May 97</td>
<td><strong>Exclusion:</strong> age &gt; 65 excluded; previous treatment with radiotherapy; previous treatment with chemotherapy</td>
<td>HU 25 mg/kg/d&lt;br&gt;Pipobroman 1.25 mg/kg/d</td>
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<td>Kiladjian et al., 2006 † (82)</td>
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<tr>
<td>Harrison et al., 2005 (85)</td>
<td>Europe</td>
<td>Aug 97–Aug 02</td>
<td><strong>Inclusion:</strong> Age at least 18 y with ET</td>
<td>HU + aspirin 75 mg/d&lt;br&gt;HU: 0.5–1 g/d&lt;br&gt;Anagrelide + aspirin 75 mg/d&lt;br&gt;anagrelide 0.5 mg BID</td>
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<tr>
<td>Finazzi Cluster/ET</td>
<td>Europe</td>
<td>Jun 05–Jun 05</td>
<td><strong>Inclusion:</strong> ET; high risk of thrombosis (&gt;60 y or prior thrombosis)</td>
<td>HU 15 mg/kg&lt;br&gt;No myelosuppressive agent at randomization†&lt;br&gt;Cortelazzo et al., 1995 (84) Aug 93–Aug 93 <strong>Inclusion:</strong> Age &gt;60; previous thrombosis; plt count &lt;1.5 million</td>
<td>HU 15 mg/kg&lt;br&gt;None</td>
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</tbody>
</table>

* In HIV, only HU doses are given.
† This was a 5-group study, but adverse event data are given for 3 groups (some groups were pooled). These are treatment-naive as well as treatment-experienced patients. Baseline data are reported for all groups combined (listed in arm 1) and were stated to be similar between arms.
‡ Randomized for 12 weeks then open-label according to response in first 12 weeks.
§ Many patients crossed over after 12 weeks—blinding removed and if poor response (viral load >200 cell/mL) permitted to start HU or dropped if already in HU arm. HU arm had 34 responders, 24 cross-overs after 3 months and 19 remaining in "placebo" arm.
¶ See reference 62 for other details of inclusion criteria—this is the same report after 24 months (instead of 12 months).
* This is a follow-up of reference 71. Very limited data is given on patients.

ANC = absolute neutrophil count; preg = pregnancy; HU = hydroxyurea; ddI = didanosine; IDV = indinavir; d4T = didehydrodeoxythymidine; ZDV = zidovudine; 3TC = lamivudine; RNA = ribonucleic acid; AST = aspartate transaminase; ALT = alanine transferase; ULT = upper limit; BID = twice a day; ABC = abacavir; EFV = efavirenz; plt = platelet; hx = history; ULN = upper limit of normal; IFN = interferon; CML = chronic myelogenous leukemia; WHO = World Health Organization; NR = not reported; WBC = white blood cells; CA = cancer; CCNU = lomustine; PV = polycythemia vera; ET = essential thrombocytopenia.
Appendix Table 4b. Description of Patient Populations in Randomized Controlled Trials on Hydroxyurea Treatment in Diseases Other than Sickle Cell Disease

<table>
<thead>
<tr>
<th>Study, Year (Reference)</th>
<th>Patient Groups/Intervention</th>
<th>Patients, n</th>
<th>Age, y*</th>
<th>Men, n (%)</th>
<th>Race, %</th>
<th>Time Point of Last Observation</th>
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<tr>
<td><strong>HIV</strong></td>
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<tr>
<td>Frank et al., 2004 (66)†</td>
<td>ddl</td>
<td>28</td>
<td>NR</td>
<td>(79)</td>
<td>White (38); Black (50); White Hispanic (10)</td>
<td>6 mo</td>
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<td></td>
<td>HU (low dose) with/without ddl</td>
<td>53</td>
<td></td>
<td>(82)</td>
<td>White (69); Black (16); White Hispanic (13)</td>
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<tr>
<td></td>
<td>HU (high dose) with/without ddl</td>
<td>50</td>
<td></td>
<td>(84)</td>
<td>White (62); Black (22); White Hispanic (12)</td>
<td></td>
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<tr>
<td>Havlir et al., 2001 (67)</td>
<td>HU IDV ddl d4T</td>
<td>68</td>
<td>NR</td>
<td>(89)</td>
<td>White (71); Black (23); White Hispanic (5)</td>
<td></td>
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<tr>
<td></td>
<td>IDV ddl d4T + placebo</td>
<td>68</td>
<td></td>
<td>(89)</td>
<td>White (71); Black (23); White Hispanic (5)</td>
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<tr>
<td></td>
<td>IDV ZDV (or d4T) 3TC</td>
<td>66</td>
<td></td>
<td>(89)</td>
<td>White (71); Black (23); White Hispanic (5)</td>
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<td>Swindells et al., 2005 (68)</td>
<td>ABC/EFV/ddl and HU</td>
<td>30</td>
<td>38.1; Median, 37 [26–59]</td>
<td>26 (87)</td>
<td>White 16, (53); Black 4, (13); White Hispanic 7, (23); Other 3, (10)</td>
<td>48 wk</td>
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<tr>
<td></td>
<td>ABC/EFV/ddl</td>
<td>24</td>
<td>39.5; Median, 37 [29–62]</td>
<td>21 (88)</td>
<td>White 13, (54); Black 8, (33); White Hispanic 2, (8); Other 1, (4)</td>
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<tr>
<td>Seminari et al., 1999 (69)</td>
<td>ddl + HU</td>
<td>40</td>
<td>33.8 [26–47]</td>
<td>26 (65)</td>
<td>NR</td>
<td>40 wk</td>
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<tr>
<td></td>
<td>ddl</td>
<td>21</td>
<td>31 [21–48]</td>
<td>13 (62)</td>
<td>NR</td>
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<td>Bloch et al., 2006 (70)</td>
<td>Indinavir/ritonavir/ddl + (either stavudine or lamivudine) and HU</td>
<td>35</td>
<td>Median, 36 [31–39]</td>
<td>NR</td>
<td>NR</td>
<td></td>
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<tr>
<td></td>
<td>Indinavir/ritonavir/ddl + (either stavudine or lamivudine)</td>
<td>33</td>
<td>Median, 34 [29–40]</td>
<td>NR</td>
<td>NR</td>
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<td><strong>Rutschmann Cluster/HIV</strong></td>
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<tr>
<td>Rutschmann et al., 1998 (71)</td>
<td>ddl/stavudine/HU</td>
<td>72</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td>24 wk</td>
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<td></td>
<td>ddI/stavudine/placebo</td>
<td>72</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
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<tr>
<td>Rutschmann et al., 1998 (72)</td>
<td>ddl/stavudine/HU</td>
<td>72</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td>48 wk</td>
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<tr>
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<td>ddI/stavudine/placebo</td>
<td>72</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
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<tr>
<td>Rutschmann et al., 2000 (73)‡</td>
<td>ddl/stavudine/HU</td>
<td>72</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td>24 mo</td>
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<tr>
<td>Study/Group</td>
<td>Treatment</td>
<td>n</td>
<td>Median, [Range]</td>
<td>m/f Ratio</td>
<td>NR</td>
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<td>-------------------------------------------------</td>
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<tr>
<td><strong>CML</strong></td>
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<tr>
<td>Hehlmann et al., 2003 (74)</td>
<td>HU</td>
<td>308</td>
<td>Median, 47 [11–83]</td>
<td>(54)</td>
<td>NR</td>
<td></td>
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<tr>
<td></td>
<td>IFN-alpha 2a + HU</td>
<td>226</td>
<td>Median, 49 [10–78]</td>
<td>(60)</td>
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<tr>
<td>Benelux CML Study Group, 1998 (75)</td>
<td>HU</td>
<td>95</td>
<td>Median, 56.4 [27–84]</td>
<td>53</td>
<td>NR</td>
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<tr>
<td></td>
<td>IFN and HU if needed</td>
<td>100</td>
<td>Median, 55.7 [20–83]</td>
<td>58</td>
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<tr>
<td>Hehlmann et al., 1994 (76)</td>
<td>HU</td>
<td>194</td>
<td>46.9; Median, 47 [15–84]</td>
<td>(51)</td>
<td>NR</td>
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<td>IFN</td>
<td>133</td>
<td>47.4; Median, 47 [18–85]</td>
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<td></td>
<td>Busulfan</td>
<td>186</td>
<td>48.5; Median, 49 [17–84]</td>
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<tr>
<td>Broustet et al., 1991 (77)</td>
<td>HU</td>
<td>26</td>
<td>58.6</td>
<td>16 (61.5)</td>
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<tr>
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<td>IFN</td>
<td>24</td>
<td>55.6</td>
<td>15 (62.5)</td>
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<tr>
<td>Hehlmann et al., 1993 (78)</td>
<td>HU</td>
<td>216</td>
<td>49.2 (unclear mean or median)</td>
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<td>NR</td>
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<td>Busulfan</td>
<td>225</td>
<td>50.2 (unclear mean or median)</td>
<td>(61)</td>
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<td><strong>Solid Tumor</strong></td>
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<tr>
<td>Stephens et al., 1984 (79)</td>
<td>HU</td>
<td>69</td>
<td>Median, 64</td>
<td>(100)</td>
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<tr>
<td></td>
<td>Adriamycin + cyclophosphamide</td>
<td>68</td>
<td>Median, 65</td>
<td>(100)</td>
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<tr>
<td>Loening et al., 1981 (80)</td>
<td>HU</td>
<td>40</td>
<td>67.3</td>
<td>(100)</td>
<td>NR</td>
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<td>Cyclophosphamide</td>
<td>43</td>
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<td>Methyl-CCNU</td>
<td>38</td>
<td>68.5</td>
<td>(100)</td>
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<td><strong>Najean Cluster/PV</strong></td>
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<tr>
<td>Najean and Rain, 1997 (81)</td>
<td>HU</td>
<td>150</td>
<td>53.2, men; 53.6, women</td>
<td>m/f ratio = 0.89</td>
<td>NR</td>
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<tr>
<td></td>
<td>Pipobroman</td>
<td>142</td>
<td>55.1, men; 53.3, women</td>
<td>m/f ratio = 1.20</td>
<td>NR</td>
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<tr>
<td>Kiladjian et al., 2006 (82)</td>
<td>HU</td>
<td>123</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
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<tr>
<td></td>
<td>Pipobroman</td>
<td>134</td>
<td>NR</td>
<td>NR</td>
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<td><strong>ET</strong></td>
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<tr>
<td>Harrison et al., 2005 (85)</td>
<td>HU + aspirin 75 mg/d</td>
<td>404</td>
<td>Median, 62 [21–88]</td>
<td>180 (45)</td>
<td>NR</td>
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<tr>
<td></td>
<td>Anagrelide + aspirin 75 mg/d</td>
<td>405</td>
<td>Median, 61 [23–88]</td>
<td>162 (40)</td>
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<tr>
<td>Finazzi et al., 2000 (83)</td>
<td>HU</td>
<td>No myelosuppressive agent at randomization</td>
<td>56</td>
<td>Median, 67 [40–82]</td>
<td>23.00</td>
<td>NR</td>
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<tr>
<td>Cortelazzo et al., 1995 (84)</td>
<td>HU</td>
<td>None</td>
<td>56</td>
<td>Median, 67</td>
<td>23.00</td>
<td>NR</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td>58</td>
<td>Median, 69 [50–85]</td>
<td>14</td>
<td>NR</td>
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</tbody>
</table>

Mean (SD) [range] unless otherwise specified.

† The characteristics represent the whole population (all three arms).

‡ Included 30 patients that crossed over to the HU arm (regrouped the arms as received HU at some point vs not), but do not report the numbers of the placebo arm. Denominators for the outcomes range from 64 to 80, because they used the numbers of patients at the time of the outcome event as denominators.

ddi = didanosine; NR = not reported; HU = hydroxyurea; IDV = indinavir; d4T = dideoxydeoxythymidine; ZDV = zidovudine; 3TC = lamivudine; ABC = abacavir; EFW = efavirenz; CML = chronic myelogenous leukemia IFN = interferon; CCNU = lomustine, m/f = male/female.
### Appendix Table 4c. Toxicity Results in Randomized Controlled Trials on Hydroxyurea Treatment in Diseases Other than Sickle Cell Disease

<table>
<thead>
<tr>
<th>Study, Year (Reference)</th>
<th>Intervention</th>
<th>N</th>
<th>Mean Duration of Drug or Follow-up</th>
<th>Deaths, n (%)</th>
<th>Neutropenia, n (%)</th>
<th>Thrombocytopenia, n (%)</th>
<th>Anemia, n (%)</th>
<th>Leukemia, n (%)</th>
<th>Other neoplasm, n (%)</th>
<th>Leg Ulcer, n (%)</th>
<th>Rash/Nail Alteration, n (%)</th>
<th>Other, n (%)</th>
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<tbody>
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<td>HIV</td>
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<tr>
<td>Frank et al., 2004† (66)</td>
<td>ddl mono</td>
<td>28</td>
<td>6 mo</td>
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<td>HU (low dose) with/without ddl</td>
<td>53</td>
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<td>HU (high dose) with/without ddl</td>
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<td>20 (40)*</td>
<td>9 (18)†</td>
<td>3 (6)</td>
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<td>Swindells et al., 2005 (68)</td>
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<td>Bloch et al., 2006 (70)</td>
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<td>Neurological/psychiatric</td>
<td>Accelerated disease/blast crisis</td>
<td>Fever</td>
<td>Thyroid insufficiency</td>
<td>CNS disturbance</td>
<td>Long-lasting BM aplasia</td>
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<td>Benelux CML Study Group, 1998 (75)</td>
<td>HU alone</td>
<td>95</td>
<td>64/22 (28.3)</td>
<td>146 (64.6)</td>
<td>82 (36.3)</td>
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<td>IFN</td>
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<td>Median follow-up: 3.4 y</td>
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<td>Treatment</td>
<td>Patients</td>
<td>Follow-up</td>
<td>NR by arm</td>
<td>GI upset</td>
<td>Myelofibrosis</td>
<td>Other Side Effects</td>
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<td>Loening et al., 1981 (80)</td>
<td>HU</td>
<td>40</td>
<td>2/28 (7)</td>
<td>2/34 (5)</td>
<td>GI upset: 13 (46) (denominator = 28)</td>
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<td>GI upset: 20 (46) (denominator = 43)</td>
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<td>Methyl-CCNU</td>
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<td>9/27 (33)</td>
<td>GI upset: 11 (41) (denominator = 27)</td>
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<td>Follow-up: 1 - 17 y</td>
<td>NR by arm</td>
<td>GI upset: 9 (7) Myelofibrosis: 26: 40% at the 16th year Cystitis: 3 (2) Stomatitis: 13 (10)</td>
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<td>NR by arm</td>
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<td>Kiladjian et al., 2006 (82)</td>
<td>HU</td>
<td>123§§</td>
<td>Follow-up: 14 y</td>
<td>15††††</td>
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<td>Pipobroman</td>
<td>134§§</td>
<td>Follow-up: 11 y</td>
<td>25***</td>
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<td>ET</td>
<td>HU + aspirin</td>
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<td>Median follow-up: 39 mo (12–72)</td>
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<td>Myelofibrosis: 5</td>
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<td>Anagrelide + aspirin</td>
<td>405</td>
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<td>4***</td>
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<td>Finazzi Cluster/ET</td>
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<td>Median follow-up: 73 mo (3-93)</td>
<td>7 (13)</td>
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<td>No myelosuppressive agent at randomization</td>
<td>58</td>
<td>Median follow-up: 73 mo (12-94)</td>
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<td>Cortelazzo et al., 1995 (84)</td>
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<td>27 mo</td>
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*P = 0.007 (comparing arms 2 and 3).
† P = NS.
‡ P = 0.04 for grade 1, ns for 2, 3, (denominator = 36).
§ P = 0.03 for grade 1, ns for 2 and 3.
\[ P = 0.7. \]
\[ P = 0.09. \]
\[ n = \text{original assignments please see associated text for number of patients that crossed over.} \]
\[ ** P = 0.04, (\text{denominator for this outcome unclear given crossover}). \]
\[ † P = 0.03. \]
\[ †† P = 0.02. \]
\[ ††† P = 0.2. \]
\[ †† † P = 0.008. \]
\[ †† † † P = 0.08. \]
\[ †† † † † P = 0.001. \]
\[ ††† † P = 0.2. \]
\[ ††† † † P = 0.006. \]
\[ ††† † † † P = 0.0321. \]
\[ †††† 6 (40\%) occurred after the 12th y of follow-up (denominator = 123). \]
\[ ††† † 11 (44\%) after the 12th y of follow-up (denominator = 134). \]
\[ †††† † † † † P = 0.001. \]
\[ † † † † † Risk = 10\% at 13th year (denominator = 150). \]
\[ † † † † † † Risk = 15\% at 14th year, Risk = 1.1\% per year. \]
\[ † † † † † † † Risk = 10\% at 13th year (denominator = 142). \]
\[ † † † † † † † † Risk = 15\% at 14th year, Risk = 1.1\% per year. \]
\[ † † † † † † † † † P = 0.0321. \]
\[ † † † † † † † † † † P = NS. \]
\[ † † † † † † † † † † † † Risk = 10\% at 13th year (denominator = 142). \]
\[ † † † † † † † † † † † † † Risk = 15\% at 14th year, Risk = 1.1\% per year. \]
\[ † † † † † † † † † † † † † † † P = 0.0321. \]
\[ † † † † † † † † † † † † † † † † P = NS. \]
\[ † † † † † † † † † † † † † † † † † P = 0.001. \]

ddl = didanosine; HU = hydroxyurea; IDV = indinavir; d4T = didehydrodeoxythymidine; GI = gastrointestinal; ZDV = zidovudine; 3TC = Lamivudine; ABC = abacavir ; EFV = efavirenz; ARV = antiretroviral; CMV = cytomegalovirus; IFN = interferon; BM = bone marrow; CNS = central nervous system; NR = not reported; CCNU = lomustine; PV = polycythemia vera; ET = essential throbocytopenia; NS = not significant; OR = odds ratio; CI = confidence interval.