## **Supplemental material/Appendix**

Table A - 1: Top-down calculation of the r/r DLBCL target population in base case analysis and scenario analysis

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| Base Case | **year 0** | **year 1** | **year 2** | **year 3** | **year 4** | **year 5** |
| German total population | 83,495,000 | 83,591,000 | 83,654,000 | 83,682,000 | 83,674,000 | 83,631,000 |
| Population ≥ 18 | 69,698,000 | 69,726,000 | 69,708,000 | 69,658,000 | 69,600,000 | 69,526,000 |
| Incident DLBCL cases | 5,158 | 5,264 | 5,368 | 5,468 | 5,575 | 5,680 |
| **Minimum Population** | | | | | | |
| 2nd line population | 1,444 | 1,474 | 1,503 | 1,531 | 1,561 | 1,590 |
| 3rd line population | 895 | 913 | 931 | 948 | 967 | 985 |
| Target population\* | 788 | 803 | 819 | 834 | 851 | 867 |
| **Maximum Population** | | | | | | |
| 2nd line population | 1,960 | 2,000 | 2,040 | 2,078 | 2,119 | 2,158 |
| 3rd line population | 1,214 | 1,239 | 1,263 | 1,287 | 1,312 | 1,337 |
| Target population\* | 1,068 | 1,090 | 1,111 | 1,133 | 1,155 | 1,177 |
| Scenario analysis | **year 0** | **year 1** | **year 2** | **year 3** | **year 4** | **year 5** |
| **Minimum Population** |  |  |  |  |  |  |
| 2nd line population | 1,444 | 1,474 | 1,503 | 1,531 | 1,561 | 1,590 |
| Target population\* | 1,271 | 1,297 | 1,323 | 1,347 | 1,374 | 1,399 |
| **Maximum Population** |  |  |  |  |  |  |
| 2nd line population | 1,960 | 2,000 | 2,040 | 2,078 | 2,119 | 2,158 |
| Target population\* | 1,725 | 1,760 | 1,795 | 1,829 | 1,865 | 1,899 |
| DLBCL, diffuse large B-cell lymphoma  \*Statutory insured | | | | | | |

Table A - 2: Calculation of the 3rd line population (minimum population)

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Clinical outcomes** | **Percentage** | **year 0** | **year 1** | **year 2** | **year 3** | **year 4** | **year 5** | **Sources** |
| **1st line** |  | 5,158 | 5,264 | 5,368 | 5,468 | 5,575 | 5,680 |  |
| Early mortality chemotherapy | 2% | 103 | 105 | 107 | 109 | 112 | 114 | Based on experts |
| Cured with R-CHOP (chemotherapy) | 70% | 3,611 | 3,685 | 3,758 | 3,828 | 3,903 | 3,976 | [6] |
| **2nd line** | 28% | 1,444 | 1,474 | 1,503 | 1,531 | 1,561 | 1,590 |  |
| **ASCT eligible** | 50% | 722 | 737 | 752 | 766 | 781 | 795 | [40] |
| Early mortality chemotherapy | 2% | 14 | 15 | 15 | 15 | 16 | 16 | Based on experts |
| Salvage – ORR | 63% | 455 | 464 | 473 | 482 | 492 | 501 | [41] |
| Salvage – Death**1** | 29% | 132 | 135 | 137 | 140 | 143 | 145 |  |
| Salvage – PFS | 50% | 227 | 232 | 237 | 241 | 246 | 250 | [41] |
| Salvage – PPS**2** | 21% | 96 | 97 | 99 | 101 | 103 | 105 |  |
| Salvage - no ORR**3** | 35% | 253 | 258 | 263 | 268 | 273 | 278 |  |
| **HDT/ASCT** | 35% | 80 | 81 | 83 | 84 | 86 | 88 | [42] |
| Early mortality ASCT | 5% | 4 | 4 | 4 | 4 | 4 | 4 | [40]**4** |
| HDT/ASCT – ORR | 70.50% | 56 | 57 | 58 | 60 | 61 | 62 | [42] |
| Salvage – Death**1** | 16% | 9% | 9% | 9% | 10% | 10% | 10% |  |
| HDT/ASCT – PFS | 65.50% | 37 | 38 | 38 | 39 | 40 | 40 | [43] |
| HDT/ASCT – PPS**2** | 18.50% | 10 | 11 | 11 | 11 | 11 | 11 |  |
| HDT/ASCT - no ORR**3** | 24.50% | 20 | 20 | 20 | 21 | 21 | 21 |  |
| **No HDT/ASCT** | 65% | 148 | 151 | 154 | 157 | 160 | 163 | [42] |
| **ASCT ineligible** | 50% | 722 | 737 | 752 | 766 | 781 | 795 | [40] |
| Early mortality chemotherapy | 2% | 14 | 15 | 15 | 15 | 16 | 16 | Based on experts |
| Salvage – ORR | 61% | 440 | 450 | 458 | 467 | 476 | 485 | [10] |
| Salvage – Death**1** | 51% | 225 | 229 | 234 | 238 | 243 | 247 |  |
| Salvage – PFS | 26% | 115 | 117 | 119 | 121 | 124 | 126 | [10] |
| Salvage – PPS**2** | 23% | 101 | 103 | 105 | 107 | 110 | 112 |  |
| Salvage - no ORR**3** | 37% | 267 | 273 | 278 | 283 | 289 | 294 |  |
| **3rd line\*** |  | 895 | 913 | 931 | 948 | 967 | 985 |  |
| ASCT, autologous stem cell transplantation; HDT, high dose (chemo) therapy; ORR, overall response rate; PFS, progression-free survival; PPS, post-progression survival; R-CHOP indicates rituximab – cyclophosphamide, doxorubicin, vincristine, prednisolone  **Part of 3rd line therapy:**  ASCT eligible: Salvage PPS + Salvage no ORR  HDT/ASCT: Salvage PPS + Salvage no ORR + HDT/ASCT no ORR  ASCT ineligible: Salvage PPS + Salvage no ORR  **1**Calculation: death = 1-OS  **2**Calculation: PPS = OS -PFS  **3**Calculation: no ORR = 1-ORR-early mortality  **4**Confirmed by experts  \*Sum may not add up to the total (3rd line) due to rounding | | | | | | | | | |

Table A - 3: Calculation of the 3rd line population (maximum population)

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Clinical outcomes** | **Percentage** | **year 0** | **year 1** | **year 2** | **year 3** | **year 4** | **year 5** | **Sources** |
| **1st line** |  | 5,158 | 5,264 | 5,368 | 5,468 | 5,575 | 5,680 |  |
| Early mortality chemotherapy | 2% | 103 | 105 | 107 | 109 | 112 | 114 | Based on experts |
| Cured with R-CHOP (chemotherapy) | 60% | 3,095 | 3,158 | 3,221 | 3,281 | 3,345 | 3,408 | [6] |
| **2nd line** | 38% | 1,960 | 2,000 | 2,040 | 2,078 | 2,119 | 2,158 |  |
| **ASCT eligible** | 50% | 980 | 1,000 | 1,020 | 1,039 | 1,059 | 1,079 | [40] |
| Early mortality chemotherapy | 2% | 20 | 20 | 20 | 21 | 21 | 22 | Based on experts |
| Salvage – ORR | 63% | 617 | 630 | 643 | 655 | 667 | 680 | [41] |
| Salvage – Death**1** | 29% | 179 | 183 | 186 | 190 | 194 | 197 |  |
| Salvage – PFS | 50% | 309 | 315 | 321 | 327 | 334 | 340 | [41] |
| Salvage – PPS**2** | 21% | 130 | 132 | 135 | 137 | 140 | 143 |  |
| Salvage – no ORR**3** | 35% | 343 | 350 | 357 | 364 | 371 | 378 |  |
| **HDT/ASCT** | 35% | 108 | 110 | 112 | 115 | 117 | 119 | [42] |
| Early mortality ASCT | 5% | 5 | 6 | 6 | 6 | 6 | 6 | [40]**4** |
| HDT/ASCT – ORR | 70.50% | 76 | 78 | 79 | 81 | 82 | 84 | [42] |
| Salvage – Death**1** | 16% | 12 | 12 | 13 | 13 | 13 | 13 |  |
| HDT/ASCT – PFS | 65.50% | 50 | 51 | 52 | 53 | 54 | 55 | [43] |
| HDT/ASCT – PPS**2** | 18.50% | 14 | 14 | 15 | 15 | 15 | 16 |  |
| HDT/ASCT – no ORR**3** | 24.50% | 26 | 27 | 28 | 28 | 29 | 29 |  |
| **No HDT/ASCT** | 65% | 201 | 205 | 209 | 213 | 217 | 221 | [42] |
| **ASCT ineligible** | 50% | 980 | 1,000 | 1,020 | 1,039 | 1,059 | 1,079 | [40] |
| Early mortality chemotherapy | 2% | 20 | 20 | 20 | 21 | 21 | 22 | Based on experts |
| Salvage – ORR | 61% | 598 | 610 | 622 | 634 | 646 | 658 | [10] |
| Salvage – Death**1** | 51% | 305 | 311 | 317 | 323 | 330 | 336 |  |
| Salvage – PFS | 26% | 155 | 159 | 162 | 165 | 168 | 171 | [10] |
| Salvage – PPS**2** | 23% | 137 | 140 | 143 | 146 | 149 | 151 |  |
| Salvage – no ORR**3** | 37% | 363 | 370 | 377 | 384 | 392 | 399 |  |
| **3rd line\*** |  | 1,214 | 1,239 | 1,263 | 1,287 | 1,312 | 1,337 |  |
| ASCT, Autologous stem cell transplantation; HDT, high dose (chemo) therapy; ORR, overall response rate; PFS, progression-free survival; PPS, post-progression survival; R-CHOP indicates rituximab – cyclophosphamide, doxorubicin, vincristine, prednisolone  **Part of 3rd line therapy:**  ASCT eligible: Salvage PPS + Salvage no ORR  HDT/ASCT: Salvage PPS + Salvage no ORR + HDT/ASCT no ORR  ASCT ineligible: Salvage PPS + Salvage no ORR  **1**Calculation: death = 1-OS  **2**Calculation: PPS = OS -PFS  **3**Calculation: no ORR = 1-ORR-early mortality  **4**Confirmed by experts  \*Sum may not add up to the total (3rd line) due to rounding | | | | | | | | |

Table A - 4: Proportion of patients treated with CAR-T cells and standard therapy

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
|  | **year 0** | **year 1** | **year 2** | **year 3** | **year 4** | **year 5** |
| **CAR-T cell therapy1** | 16.50% | 20.30% | 24.96% | 30.70% | 37.77% | 46.45% |
| **Standard therapy** | 83.50% | 79.70% | 75.04% | 69.30% | 62.23% | 53.55% |
| **Total** | 100.00% | 100.00% | 100.00% | 100.00% | 100.00% | 100.00% |
| CAR, chimeric antigen receptor  **1**Equal shares for Tisa-cel and Axi-cel | | | | | | |

Table A - 5: Number of patients treated with CAR-T and standard therapy in base case analysis

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| Base case analysis | **year 0** | **year 1** | **year 2** | **year 3** | **year 4** | **year 5** |
| **Minimum Population** |  |  |  |  |  |  |
| Axicabtagene Ciloleucel | 65 | 81 | 102 | 128 | 161 | 201 |
| Tisagenlecleucel | 65 | 81 | 102 | 128 | 161 | 201 |
| Standard therapy | 658 | 640 | 615 | 578 | 530 | 464 |
| Total\* | 788 | 803 | 819 | 834 | 851 | 867 |
| **Maximum Population** |  |  |  |  |  |  |
| Axicabtagene Ciloleucel | 88 | 111 | 139 | 174 | 218 | 273 |
| Tisagenlecleucel | 88 | 111 | 139 | 174 | 218 | 273 |
| Standard therapy | 892 | 869 | 834 | 785 | 719 | 630 |
| Total\* | 1,068 | 1,090 | 1,111 | 1,133 | 1,155 | 1,177 |
| Scenario analysis | **year 0** | **year 1** | **year 2** | **year 3** | **year 4** | **year 5** |
| **Minimum Population** |  |  |  |  |  |  |
| Axicabtagene Ciloleucel | 105 | 132 | 165 | 207 | 259 | 325 |
| Tisagenlecleucel | 105 | 132 | 165 | 207 | 259 | 325 |
| Standard therapy | 1,061 | 1,034 | 993 | 933 | 855 | 749 |
| Total\* | 1,271 | 1,297 | 1,323 | 1,347 | 1,374 | 1,399 |
| **Maximum Population** |  |  |  |  |  |  |
| Axicabtagene Ciloleucel | 142 | 179 | 224 | 281 | 352 | 441 |
| Tisagenlecleucel | 142 | 179 | 224 | 281 | 352 | 441 |
| Standard therapy | 1,440 | 1,403 | 1,347 | 1,267 | 1,161 | 1,017 |
| Total\* | 1,725 | 1,760 | 1,795 | 1,829 | 1,865 | 1,899 |
| **\***Sum may not add up to the total due to rounding | | | | | | |

Table A - 6: Annual costs and budget impact in base case analysis

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| Base case analysis (Costs in €) | **year 0** | **year 1** | **year 2** | **year 3** | **year 4** | **year 5** |
| **Minimum Population** | | | | | | |
| Costs without CAR-T | 44,304,512 | 45,147,872 | 46,047,456 | 46,890,816 | 47,846,624 | 48,746,208 |
| Costs with CAR-T | 83,724,075 | 94,556,892 | 108,031,471 | 124,527,498 | 145,286,245 | 170,850,305 |
| Budget Impact | 39,419,562 | 49,409,020 | 61,984,015 | 77,636,682 | 97,439,621 | 122,104,097 |
| Cumulative budget impact | 447,992,998 |  |  |  |  |  |
| **Maximum Population** | | | | | | |
| Costs without CAR-T | 60,047,232 | 61,284,160 | 62,464,864 | 63,701,792 | 64,938,720 | 66,175,648 |
| Costs with CAR-T | 113,473,746 | 128,352,443 | 146,548,186 | 169,172,249 | 197,186,385 | 231,938,649 |
| Budget Impact | 53,426,514 | 67,068,283 | 84,083,322 | 105,470,457 | 132,247,665 | 165,763,001 |
| Cumulative budget impact | 608,059,242 |  |  |  |  |  |
| Scenario analysis (Costs in €) | **year 0** | **year 1** | **year 2** | **year 3** | **year 4** | **year 5** |
| **Minimum Population** |  |  |  |  |  |  |
| Costs without CAR-T | 56,877,250 | 58,040,750 | 59,204,250 | 60,278,250 | 61,486,500 | 62,605,250 |
| Costs with CAR-T | 122,865,073 | 140,866,111 | 163,121,661 | 190,415,367 | 224,763,657 | 267,090,281 |
| Budget Impact | 65,987,823 | 82,825,361 | 103,917,411 | 130,137,117 | 163,277,157 | 204,485,031 |
| Cumulative budget impact | 750,629,900 |  |  |  |  |  |
| **Maximum Population** |  |  |  |  |  |  |
| Costs without CAR-T | 77,193,750 | 78,760,000 | 80,326,250 | 81,847,750 | 83,458,750 | 84,980,250 |
| Costs with CAR-T | 166,752,361 | 191,152,163 | 221,317,749 | 258,552,120 | 305,083,129 | 362,547,851 |
| Budget Impact | 89,558,611 | 112,392,163 | 140,991,499 | 176,704,370 | 221,624,379 | 277,567,601 |
| Cumulative budget impact | 1,018,838,624 |  |  |  |  |  |
| CAR, chimeric antigen receptor |  |  |  |  |  |  |