

****Published October 2017****

MarketVIEW: CAR-T r/r CLL global¹ market forecast (CAT: IOMV076)

Product Name	:	MarketVIEW: CAR-T r/r Chronic lymphocytic leukaemia (CLL) commercial market forecast
Description	:	Commercial assessment of new CAR-T therapies in relapsed/refractory CLL
Contents	:	Executive presentation [~130 slides] + 1 MS Excel workbook
Therapeutic Area	:	Cancer immunotherapy
Publication date	:	October 2017
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Background

Chronic lymphocytic leukaemia (CLL) is the most common type of leukaemia in western countries with an age-adjusted incidence of ~4.4 per 100,000 persons in the United States. In 2017, the US recorded ~20,000 diagnosed cases and ~4,600 deaths. Global¹ estimates are ~36,000 diagnosed cases per year.

Symptomatic CLL disease remains incurable with standard therapies although HSCT can offer a cure, dependent on patient age; comorbidity and the potential for GvHD. Recent improvements in standard (chemo-immunotherapeutic) therapy have been achieved with small molecule inhibitors of B cell receptor signalling such as Ibrutinib (Imbruvica®, AbbVie, Janssen) (a Bruton's Tyrosine Kinase (BTK) inhibitor) and Idelalisib (Zydelig®, Gilead) (a PI3K δ -isoform selective inhibitor) and the apoptosis regulation inhibitor Venetoclax (Venclexta®, Abbvie, Genentech Roche) (an inhibitor of B-cell lymphoma-2 (BCL-2)). Despite their benefits these agents require continuous administration and are not curative. BTK refractory CLL remains an issue. High risk patients with cytogenetic aberrations (e.g. del(17p), del(11q), TP53 mutation, unmutated IGHV) have a poor prognosis and unfavourable/short outcomes.

Novel immune-therapeutic approaches in development for CLL include monoclonal antibodies, bi-specific antibodies, anti-PD-1/PDL-1 checkpoint inhibitors, and the CAR-T cell therapies including **JCAR014/JCAR017 (Juno Therapeutics)**, **KTE-C19 (Kite Pharma)**, and **CTL019 (tisagenlecleucel-T) (Novartis Pharmaceuticals)**. These potential CAR-T therapies or their next generations e.g. 'armoured' CARs and humanized versions are in development.

This **MarketVIEW** product consists of a detailed Executive presentation (~130 slides, .pdf) and MS-Excel workbook forecasting the commercial potential (\$ 000s) of novel CAR-T therapies in r/r CLL across 9 major Western¹ markets to 2030. A patient-based flow methodology has been devised where **possible intervention scenarios** for CAR-T introduction are visualised so that the optimum product positioning can be assessed. In addition, an up-to-date review of CLL disease background, epidemiology, current and future treatments is presented along with a comprehensive review of the CAR-T CLL competitive

¹ US, Canada, UK, France, Germany, Italy, Spain, UK, Australia and Japan

landscape. Pricing, cost effectiveness, manufacturing and logistical considerations are also discussed. All assumptions are clearly provided.

Methodology

iOnco Analytics has closely monitored all significant source material pertaining to CLL and CAR-T therapies as approaches to cancer immunotherapy. Source materials used are literature articles, government websites, medical bodies and associations, conference proceedings etc.

PRODUCT CONTENTS:

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****This product is composed of [one Excel workbook \(.xls\)](#)² and [an Executive Presentation \(.pdf\)](#)³

Executive summary

CAR-T treatment for r/r CLL - Commercial model: key outputs

- CAR-T eligible CLL patients/line of therapy 2017-2030 (Global¹)
- CAR-T eligible CLL patients/line of therapy to 2030 (US)
- CAR-T eligible CLL patients/line of therapy to 2030 (M5EU)
- CAR-T treated CLL patients/line of therapy to 2030 (Global¹)
- CAR-T treated CLL patients/line of therapy to 2030 (US)
- CAR-T treated CLL patients/line of therapy to 2030 (M5EU)
- CAR-T cell therapy: projected CLL revenue forecast per scenario (\$000s) to 2030 (Global¹)
- CAR-T cell therapy: projected CLL revenue forecast per scenario (\$000s) to 2030 (US)
- CAR-T cell therapy: projected CLL revenue forecast per scenario (\$000s) to 2030 (M5EU)

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- Chronic lymphocytic leukaemia (CLL) - Incidence (US)
- Chronic lymphocytic leukaemia (CLL) - Incidence, age distribution and mortality (US)
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- Chronic lymphocytic leukaemia (CLL) - Leukaemia incidence (UK)
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- Chronic lymphocytic leukaemia (CLL) - Incidence, mortality and country (UK)
- Chronic lymphocytic leukaemia (CLL) - Incidence and mortality in US, Canada, Europe, Australia, Japan
- Chronic lymphocytic leukaemia (CLL) - Prevalence in US, Canada, Europe, Australia, Japan

Chronic lymphocytic leukaemia – Treatment

- Chronic lymphocytic leukaemia (CLL) – Treatment requirements
- Chronic lymphocytic leukaemia (CLL) - Treatment agents
- Chronic lymphocytic leukaemia (CLL) - Treatment agents for relapsed/refractory CLL

² Contents available on request

³ Presentation titles may apply to more than one slide



Chronic lymphocytic leukaemia - Treatment regimens by disease stage and risk category

Chronic lymphocytic leukaemia - Treatment flow

Chronic lymphocytic leukaemia – Transplantation

Chronic lymphocytic leukaemia - Transplantation treatment scenarios

Chronic lymphocytic leukaemia - Treatment challenges

Novel treatments for CLL - Immunotherapy approaches

Chronic lymphocytic leukaemia - Immunotherapy approaches in development

Chimeric Antigen Receptor T cells (CAR-T) – overview

Chimeric Antigen Receptor T cells (CAR-T) - antigen selection

CAR-T cell therapy: potential issues and challenges

Steps in the manufacture of a CAR-T cell therapy

CAR-T cell therapy for CLL- Key published studies

CAR-T cell therapy for CLL- Key published studies - Studies in combination with ibrutinib

CAR-T cell therapy for CLL- Summary of key published studies

CAR-T cell therapy for CLL: pipeline analysis methodology

CAR-T cell therapy for CLL: pipeline analysis – key findings

Pipeline analysis table: Key ongoing CAR-T studies for CLL

Key CAR-T cell programmes - Juno Therapeutics Inc. – Background

Juno Therapeutics Inc. - Background: CAR and TCR R&D pipeline

Juno Therapeutics Inc. - Background: CAR-T manufacturing process (JCAR017)

Pipeline analysis: Key industry CAR-T studies for CLL - Juno Therapeutics

Pipeline analysis: Key industry CAR-T studies for CLL - Novartis and CTL019 background

Pipeline analysis: Key industry CAR-T studies for CLL - Novartis and CTL019 background: the path to commercialization

Pipeline analysis: Key industry CAR-T studies for CLL - Novartis and CTL019 background: manufacturing process

Pipeline analysis: Key industry CAR-T studies for CLL - Novartis and CTL019

Pipeline analysis: Key industry CAR-T studies for CLL - Novartis and CTL119 – background

Pipeline analysis: Key CAR-T studies for CLL - Novartis and CTL119

Pipeline analysis: Key CAR-T studies for CLL - Kite Pharma/Gilead and CAR-T cell therapy background

Kite Pharma/Gilead and CAR-T cell therapy - Axi-Cel (KTE-C19) manufacturing process

Kite Pharma/Gilead: CAR-T R&D pipeline, September 2017

Novel treatments for CLL - Modelling commercial potential of CAR-T cell therapies

CAR-T cell therapy for CLL: Target product profile

CAR-T cell therapy for CLL: International Workshop on Chronic Lymphocytic Leukaemia (iwCLL) guidelines

CLL modelling approach: patient flow/treatment scenarios

Modelling approach: markets modelled in this analysis

Pricing CAR-T cell therapy

Pricing CAR-T therapies for indications other than paediatric ALL

Price comparisons of existing therapies for first line and r/r CLL

US cost burden projection for CLL with oral therapies as first line treatment

Pricing comparisons with cell and novel immuno-oncology therapies

Pipeline summary/potential launch sequence

Model caveats and limitations

Bibliography

Slide number ~130

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BIBLIOGRAPHY:

1. Novartis Sets a Price of \$475,000 for CAR T-Cell Therapy. 2017. Available at: <http://www.onclive.com/web-exclusives/novartis-sets-a-price-of-475000-for-car-tcell-therapy>. Accessed Sep 2017.
2. 5 Tough Questions for Gilead Sciences About the Kite Pharma Acquisition. 2017. Available at: <https://www.fool.com/investing/2017/09/11/5-tough-questions-for-gilead-sciences-about-the-ki.aspx>. Accessed Sep 2017.
3. CHRONIC LYMPHOCYTIC LEUKEMIA Union for International Cancer Control 2014 Review of Cancer Medicines on the WHO List of Essential Medicines. Available at: http://www.who.int/selection_medicines/committees/expert/20/applications/CLL.pdf. Accessed Aug 2017.
4. Chronic lymphocytic leukemia: diagnosis and clinical staging in *Advances in the Treatment of B-cell Chronic Lymphocytic Leukaemia.*, Mulligan SP and Tam CS, Keating MJ and Tam CS, Editors. 2012, Future Medicine. p. 6-15.
5. Guidelines for the diagnosis and treatment of chronic lymphocytic leukemia: a report from the International Workshop on Chronic Lymphocytic Leukemia updating the National Cancer Institute–Working Group 1996 guidelines. Hallek et al. *Blood*. 2008; 111(12): 5446–5456.
6. Clinical utility of flow cytometry in the chronic lymphoid leukemias. DiGiuseppe and Borowitz. *Semin Oncol*. 1998;25(1):6-10.
7. Chronic Lymphocytic Leukemia Treatment (PDQ®)—Health Professional Version. Available at: https://www.cancer.gov/types/leukemia/hp/cll-treatment-pdq#cit/section_1.33. Accessed Aug 2017.
8. Chronic Lymphocytic Leukemia. Kay et al. *Hematology Am Soc Hematol Educ Program*. 2002:193-213.
9. Leukemia - Chronic Lymphocytic – CLL. Available at: <http://www.cancer.net/cancer-types/leukemia-chronic-lymphocytic-cll>. Accessed Aug 2017.
10. Chronic Lymphocytic Leukemia Treatment (PDQ®)—Patient Version. Available at: <https://www.cancer.gov/types/leukemia/patient/cll-treatment-pdq>. Accessed Aug 2017.
11. The relationship between chronic lymphocytic leukaemia and prolymphocytic leukaemia: IV. Analysis of survival and prognostic features. Melo et al. *Br J Haematol*. 1986;63:377–387.
12. Genetic lesions in chronic lymphocytic leukemia: what's ready for prime time use? Moreno et al. *Haematologica* | 2010; 95(1).
13. Should IGHV status and FISH testing be performed in all CLL patients at diagnosis? A systematic review and meta-analysis. Parikh et al. *Blood*. 2016; 127(14):1752-1760.
14. Prognostic factors in chronic lymphocytic leukemia. Hallek. *Annals of Oncology*, 2008; 19 (Supplement 4): iv51–iv53.
15. Genomic aberrations and survival in chronic lymphocytic leukemia. Döhner et al. *N Engl J Med*. 2000; 343:1910–1916.
16. Prospective evaluation of clonal evolution during long-term follow-up of patients with untreated early-stage chronic lymphocytic leukemia. Shanafelt et al. *J Clin Oncol*. 2006; 24:4634–4641.
17. Chronic lymphocytic leukemia: 2017 update on diagnosis, risk stratification, and treatment. Hallek. *Am J Hematol*. 2017; 92:946–965.
18. 11q deletions identify a new subset of B-cell chronic lymphocytic leukemia characterized by extensive nodal involvement and inferior prognosis. Dohner et al. *Blood* 1997; 89:2516–2522.
19. Unmutated Ig VH Genes Are Associated With a More Aggressive Form of Chronic Lymphocytic Leukemia. Hamblin et al. *Blood* 1999; 94(6):1848-1854.
20. Chronic Lymphocytic Leukemia: Prognostic Factors and Impact on Treatment. 2017. Parker. Available at: <http://www.discoverymedicine.com/Terri-L-Parker/2011/02/12/chronic-lymphocytic-leukemia-prognostic-factors-and-impact-on-treatment/>. Accessed Sep 2017.
21. Genetic Abnormalities in Chronic Lymphocytic Leukemia: Where We Are and Where We Go. Puiggros et al. *Biomed Res Int*. 2014;2014:435983.
22. Mutations of NOTCH1 are an independent predictor of survival in chronic lymphocytic leukemia. Rossi et al. *Blood*. 2012;119(2):521-529.
23. SF3B1 mutations in chronic lymphocytic leukemia. Wan et al. *Blood*. 2013; 121(23): 4627–4634.
24. Identifying High-Risk Chronic Lymphocytic Leukemia: A Pathogenesis-Oriented Appraisal of Prognostic and Predictive Factors in Patients Treated with Chemotherapy with or without Immunotherapy. Martinelli et al. *Mediterr J Hematol Infect Dis*. 2016; e2016047.
25. Clinical staging of chronic lymphocytic leukemia. Rai et al. *Blood*. 1975; 46 (2): 219-34.
26. A new prognostic classification of chronic lymphocytic leukemia derived from a multivariate survival analysis. Binet et al. *Cancer*. 1981; 48 (1): 198-206.
27. International C. L. L. I. P. I. working group. An international prognostic index for patients with chronic lymphocytic leukaemia (CLL-IPI): a meta-analysis of individual patient data. *Lancet Oncol*. 2016;17:779–790.
28. Cancer Stat Facts. Available at: <https://seer.cancer.gov/statfacts/>. Accessed Aug 2017.
29. Cancer Stat Facts: Chronic Lymphocytic Leukemia (CLL). <https://seer.cancer.gov/statfacts/html/clyl.html>. Accessed Aug 2017.
30. Statistics by cancer type. Available at: <http://www.cancerresearchuk.org/health-professional/cancer-statistics/statistics-by-cancer-type/>. Accessed Aug 2017.
31. GLOBOCAN 2012: Estimated cancer incidence, mortality and prevalence worldwide in 2012. Available at: http://globocan.iarc.fr/Pages/summary_table_pop_sel.aspx. Accessed Aug 2017.
32. FACTS AND STATISTICS. Available at: <https://www.ils.org/http%3A/ilsorg.prod.acquia-sites.com/facts-and-statistics/facts-and-statistics-overview/facts-and-statistics>. Accessed Sep 2017.



33. Targeted therapies predicted to blow out costs for CLL. 2017. Available at: www.mdedge.com/hematologynews/article/118611/cll/targeted-therapies-predicted-blow-out-costs-cll. Accessed Sep 2017.
34. Monoclonal B-cell lymphocytosis and chronic lymphocytic leukemia. Rawstron et al. *N Engl J Med.* 2008; 359 (6): 575-83.
35. CLL Trialists' Collaborative Group. Chemotherapeutic options in chronic lymphocytic leukemia: a meta-analysis of the randomized trials. *J Natl Cancer Inst.* 1999; 91:861-868.
36. FDA Approval for Rituximab. 2010. Available at: <https://www.cancer.gov/about-cancer/treatment/drugs/fda-rituximab#a>. Accessed Sep 2017.
37. FDA Approves Arzerra. 2009. Available at: <https://www.drugs.com/newdrugs/fda-approves-arzerra-ofatumumab-chronic-lymphocytic-leukemia-1750.html>. Accessed Sep 2017.
38. Genmab Announces U.S. FDA Approval of Arzerra (ofatumumab) as Extended Treatment for Recurrent or Progressive CLL. 2016. Available at: <https://www.drugs.com/newdrugs/genmab-announces-u-s-fda-approval-arzerra-ofatumumab-extended-recurrent-progressive-cll-4327.html>. Accessed Sep 2017.
39. Genmab Announces U.S. FDA Approval of Arzerra (ofatumumab) in Combination with Fludarabine and Cyclophosphamide for Relapsed CLL. 2016. Available at: <https://www.drugs.com/newdrugs/genmab-announces-u-s-fda-approval-arzerra-ofatumumab-combination-fludarabine-cyclophosphamide-4425.html>. Accessed Sep 2017.
40. FDA Approval for Obinutuzumab. 2013. Available at: <https://www.cancer.gov/about-cancer/treatment/drugs/fda-obinutuzumab>. Accessed Sep 2017.
41. FDA Approval for Alemtuzumab. Available at: <https://www.cancer.gov/about-cancer/treatment/drugs/fda-alemtuzumab>. Accessed Sep 2017.
42. US Campath Distribution Program. Available at: <http://www.campath.com/>. Accessed Sep 2017.
43. FDA Approves Lemtrada. 2014. Available at: <https://www.drugs.com/newdrugs/fda-approves-lemtrada-alemtuzumab-relapsing-forms-multiple-sclerosis-4110.html>. Accessed Sep 2017.
44. FDA Approves Imbruvica (ibrutinib) to Treat Chronic Lymphocytic Leukemia. 2014. Available at: <https://www.drugs.com/newdrugs/fda-approves-imbruvica-ibrutinib-chronic-lymphocytic-leukemia-4007.html>. Accessed Sep 2017.
45. FDA Expands Approved Use of Imbruvica (ibrutinib) for Chronic Lymphocytic Leukemia. 2014. Available at: <https://www.drugs.com/newdrugs/fda-expands-approved-imbruvica-ibrutinib-chronic-lymphocytic-leukemia-4061.html>. Accessed Sep 2017.
46. FDA Approves Imbruvica (ibrutinib) for the First-Line Treatment of Chronic Lymphocytic Leukemia. 2016. Available at: FDA Approves Imbruvica (ibrutinib) for the First-Line Treatment of Chronic Lymphocytic Leukemia. Accessed Sep 2017.
47. FDA Approves Zydelig. 2014. Available at: <https://www.drugs.com/newdrugs/fda-approves-zydelig-idelalisib-cll-lymphoma-4056.html>. Accessed Sep 2017.
48. FDA Approves Venclexta. 2016. Available at: <https://www.drugs.com/newdrugs/fda-approves-venclexta-venetoclax-chronic-lymphocytic-leukemia-17p-deletion-4366.html>. Accessed Sep 2017.
49. Advances in the treatment of relapsed/refractory chronic lymphocytic leukemia. Shustik et al. *Ann Hematol.* 2017; 96(7):1185-1196.
50. Ibrutinib (Imbruvica): A Novel Targeted Therapy for Chronic Lymphocytic Leukemia. Parmar et al. *P T.* 2014; 39(7): 483-487, 519.
51. Idelalisib and Rituximab in Relapsed Chronic Lymphocytic Leukemia. Furman et al. *N Engl J Med.* 2014; 370(11): 997-1007.
52. Targeting BCL-2 in B-cell lymphomas. Davids. *Blood.* 2017;130(9):1081-1088.
53. FDA Grants Full Approval to Ofatumumab (Arzerra) for CLL. Available at: <http://www.medscape.com/viewarticle/823837>. Accessed Aug 2017.
54. US Campath Distribution Program. Available at: <http://www.campath.com/>. Accessed Aug 2017.
55. CLL therapy: progress at last! Montserrat E. *Blood.* 2005; 105(1):2-3.
56. Chronic Lymphocytic Leukemia Treatment Protocols. Available at: <http://emedicine.medscape.com/article/2005390-overview>. Accessed Aug 2017.
57. Pentostatin treatment combinations in chronic lymphocytic leukemia. Lamanna and Kay. *Clin Adv Hematol Oncol.* 2009; 7(6):386-92.
58. Bendamustine compared with chlorambucil in previously untreated patients with chronic lymphocytic leukaemia: updated results of a randomized phase III trial. Knauf et al. *Br J Haematol.* 2012; 159(1):67-77.
59. Alemtuzumab (Campath-1H) in the treatment of chronic lymphocytic leukemia. Alinari. *Oncogene* (2007) 26, 3644-3653.
60. Obinutuzumab in chronic lymphocytic leukemia: design, development and place in therapy. Al-Sawaf et al. *Drug Des Devel Ther.* 2017 Jan 25;11:295-304
61. U.S. Food and Drug Administration approval: ofatumumab for the treatment of patients with chronic lymphocytic leukemia refractory to fludarabine and alemtuzumab. Lemery et al. *Clin Cancer Res.* 2010; 16(17):4331-8.
62. Health-Related Quality of Life and Patient-Reported Outcomes in Patients Receiving Ofatumumab in Combination with Fludarabine and Cyclophosphamide (FC) Versus FC Alone in the Complement 2 Trial. Robak et al. *Blood* 2015 126:5288.
63. Ibrutinib as Initial Therapy for Patients with Chronic Lymphocytic Leukemia. Burger et al. *N Engl J Med.* 2015; 373(25):2425-37.
64. Targeting BTK with Ibrutinib in Relapsed Chronic Lymphocytic Leukemia. Byrd et al. *N Engl J Med.* 2013; 369(1): 32-42.

65. Ibrutinib versus Ofatumumab in Previously Treated Chronic Lymphoid Leukemia. Byrd et al. *N Engl J Med.* 2014; 371(3): 213–223.
66. Venetoclax package insert. Available at: https://www.accessdata.fda.gov/drugsatfda_docs/label/2016/208573s000lbl.pdf. Accessed Aug 2017.
67. NCCN Clinical Practice Guidelines in Oncology. Available at: https://www.nccn.org/professionals/physician_gls/pdf/cll.pdf. Accessed Aug 2017.
68. Lenalidomide and Rituximab for the Initial Treatment of Patients With Chronic Lymphocytic Leukemia: A Multicenter Clinical-Translational Study From the Chronic Lymphocytic Leukemia Research Consortium. James et al. *J Clin Oncol.* 2014; 32:2067-2073.
69. Comorbidity and functional status are independent in older patients. Extermann et al. *J Clin Oncol.* 1998; 16:1582–1587.
70. Managing high-risk CLL during transition to a new treatment era: stem cell transplantation or novel agents? Dreger et al. *Blood.* 2014; 124(26): 3841–3849.
71. How will B-cell-receptor-targeted therapies change future CLL therapy? Jones and Byrd. *Blood.* 2014; 123(10):1455–1460.
72. Clinical practice recommendations for use of allogeneic hematopoietic cell transplantation in chronic lymphocytic leukemia on behalf of the guidelines Committee of the American Society for blood and marrow transplantation. Kharfane-Dabaja et al. 2016; *Biol Blood Marrow Transplant* 22(12):2117–2125.
73. Risk stratification in chronic lymphocytic leukemia. Seiler et al. *Semin Oncol.* 2006; 33(2):186-94.
74. Prognostic subgroups in B-cell chronic lymphocytic leukemia defined by specific chromosomal abnormalities. Juliusson et al. *N Engl J Med.* 1990; 323(11): 720-4.
75. Prognostic significance of chromosome abnormalities in chronic lymphocytic leukaemia. Pittman and Catovsky. *Br J Haematol.* 1984; 58(4):649-60.
76. In B-cell chronic lymphocytic leukaemia chromosome 17 abnormalities and not trisomy 12 are the single most important cytogenetic abnormalities for the prognosis: a cytogenetic and immunophenotypic study of 480 unselected newly diagnosed patients. Geisler et al. *Leuk Res.* 1997; 21(11-12):1011-23.
77. Risk categories and refractory CLL in the era of chemoimmunotherapy. Zenz et al. *Blood.* 2012; 119(18):4101-7.
78. TP53 mutation and survival in chronic lymphocytic leukemia. Zenz T et al. *J Clin Oncol.* 2010; 28(29):4473-4479.
79. Clonal evolution in CLL patients as detected by FISH versus chromosome banding analysis, and its clinical significance. Wawrzyniak et al. *The European Journal of Haematology.* 2014; 92(2): 91–101.
80. De novo deletion 17p13.1 chronic lymphocytic leukemia shows significant clinical heterogeneity: the M. D. Anderson and Mayo Clinic experience. 2009. Tam et al. *Blood:* 114 (5); 957–964
81. Idelalisib, an inhibitor of phosphatidylinositol 3-kinase p110delta, for relapsed/refractory chronic lymphocytic leukemia. 2014. Brown et al. *Blood:* 123;3390–3397
82. Targeting BCL2 with venetoclax in relapsed chronic lymphocytic leukemia. 2016. Roberts et al. *N Engl J Med:* 374; 311–322.
83. Venetoclax in Patients with Previously Treated Chronic Lymphocytic Leukemia. 2017. Roberts et al. *Clin Cancer Res:* 23(16); 4527–33.
84. Venetoclax in relapsed or refractory chronic lymphocytic leukaemia with 17p deletion: a multicentre, open-label, phase 2 study. 2016. Stilgenbauer. *Lancet Oncol:* 17(6); 768-778.
85. Venetoclax (VEN) monotherapy for patients with chronic lymphocytic leukemia (CLL) who relapsed after or were refractory to ibrutinib or idelalisib [abstract]. 2016. Jones et al. *Blood:* 128(22). Abstract 637.
86. How I manage ibrutinib-refractory chronic lymphocytic leukemia. Woyach. *Blood.* 2017; 129(10):1270-1274.
87. Ibrutinib for patients with relapsed or refractory chronic lymphocytic leukaemia with 17p deletion (RESONATE-17): a phase 2, open-label, multicentre study. O'Brien et al. *Lancet Oncol.* 2016; 17(10):1409-1418.
88. Outcomes of CLL patients treated with sequential kinase inhibitor therapy: a real world experience. Mato et al. *Blood;* 2016;128(18):2199-2205.
89. Frontline CLL Therapy: Changes in Paradigm. 2017. Rai. Available at: <http://www.cancernetwork.com/article/frontline-cll-therapy-changes-paradigm>. Accessed Sep 2017.
90. Venetoclax for the treatment of patients with chronic lymphocytic leukemia. Crombie et al. *Future Oncol* 2017; 3(14):1223-1232.
91. Study to Evaluate Efficacy and Safety of MOR208 With Idelalisib or Venetoclax in R/R CLL/SLL Patients Pretreated With BTKi (COSMOS). Available at: <https://clinicaltrials.gov/ct2/show/NCT02639910?term=NCT02639910&rank=1>. Accessed Aug 2017.
92. Intravenous BI 836826 in Combination With Ibrutinib in Relapsed/Refractory Chronic Lymphocytic Leukemia (CLL) Patients Who Have Received at Least One Prior Systemic Therapy, and Who Are Eligible for Treatment With Ibrutinib. Available at: <https://clinicaltrials.gov/ct2/show/NCT02759016?term=NCT02759016&rank=1>. Accessed Aug 2017.
93. A Safety and Pharmacokinetic Study of BTCT4465A, With or Without Single-dose Obinutuzumab Pretreatment, in Non-Hodgkin's Lymphoma (NHL) and Chronic Lymphocytic Leukemia (CLL). Available at: <https://clinicaltrials.gov/ct2/show/NCT02500407?term=NCT02500407&rank=1>. Accessed Aug 2017.



94. Nivolumab With Ibrutinib for Relapsed, Refractory or High-Risk Untreated Patients With Chronic Lymphocytic Leukemia (CLL). Available at <https://clinicaltrials.gov/ct2/show/NCT02420912?term=NCT02420912&rank=1>. Accessed Aug 2017.
95. Pembrolizumab Alone or With Idelalisib or Ibrutinib in Treating Patients With Relapsed or Refractory Chronic Lymphocytic Leukemia or Other Low-Grade B-Cell Non-Hodgkin Lymphomas. Available at: <https://clinicaltrials.gov/ct2/show/NCT02332980?term=NCT02332980&rank=1>. Accessed Aug 2017.
96. Study of Pembrolizumab in Combination With Ublituximab and TGR-1202 in Patients With Relapsed-refractory CLL or Richter's Transformation. Available at: <https://clinicaltrials.gov/ct2/show/NCT02535286?term=NCT02535286&rank=1>. Accessed Aug 2017.
97. A Study to Determine Dose, Safety, and Efficacy of Durvalumab as Monotherapy and in Combination Therapy in Subjects With Lymphoma or Chronic Lymphocytic Leukemia (FUSION NHL 001). Available at: <https://clinicaltrials.gov/ct2/show/NCT02733042?term=NCT02733042&rank=1>. Accessed Aug 2017.
98. Atezolizumab (PD-L1 mAb) in Combination With Obinutuzumab and Ibrutinib in Patients With Relapsed Refractory or High-Risk Untreated Chronic Lymphocytic Leukemia (CLL). Available at: <https://clinicaltrials.gov/ct2/show/NCT02846623?term=NCT02846623&rank=1>. Accessed Aug 2017.
99. Patient-individualized Peptide Vaccination in Combination With Lenalidomide After First Line Therapy of CLL. Available at: <https://clinicaltrials.gov/ct2/show/NCT02802943>. Accessed Aug 2017.
100. Expression of immunoglobulin-T-cell receptor chimeric molecules as functional receptors with antibodytype specificity. Gross et al. Proc Natl Acad Sci USA. 1989; 86(24):10024-10028.
101. Manufacturing validation of biologically functional T cells targeted to CD19 antigen for autologous adoptive cell therapy. Hollyman et al. J Immunother. 2009; 32(2):169-80.
102. Chimeric antigen receptor therapy for cancer. Barrett et al. Annu Rev Med. 2014; 65:333-47.
103. CD28 costimulation improves expansion and persistence of chimeric antigen receptor-modified T cells in lymphoma patients. Savoldo et al. J Clin Invest. 2011; 121(5): 1822-1826.
104. Eradication of B-lineage cells and regression of lymphoma in a patient treated with autologous T cells genetically engineered to recognize CD19. Kochenderfer et al. Blood. 2010; 16(20):4099-4102.
105. Chimeric Antigen Receptor T Cells for Sustained Remissions in Leukemia. Maude e al. N Engl J Med. 2014; 371(16): 1507-1517.
106. CD19-CAR Trials. Ramos et al. Cancer J. 2014; 20(2): 112-118.
107. CD19 antigen in leukemia and lymphoma diagnosis and immunotherapy. Scheuermann and Racila. 1995. Leuk Lymphoma. 18(5-6):385-97.
108. Construction of anti-CD20 single-chain antibody-CD28-CD137-TCR ζ recombinant genetic modified T cells and its treatment effect on B cell lymphoma. Chen et al. 2015. Med Sci Monit, 21 p2110-2115.
109. Treatment of CD33-directed chimeric antigen receptor-modified T cells in one patient with relapsed and refractory acute myeloid leukemia. Wang et al. 2015. Mol Ther, 23:184-191.
110. Diverse solid tumors expressing a restricted epitope of L1-CAM can be targeted by chimeric antigen receptor redirected T lymphocytes. Hong et al. 2014. J Immunother, 37:93-104.
111. Chimeric antigen receptor (CAR) T cell therapy for malignant cancers: Summary and perspective. Aaron J. Smith. 2016. J. of Cellular Immunotherapy, 2:59-68.
112. Genetically modified T cells in cancer therapy: opportunities and challenges. Sharpe and Mount. 2015. Dis Model Mech. Apr; 8(4): 337-350.
113. Toxicities of chimeric antigen receptor T cells: recognition and management. Brudno and Kochenderfer. 2016. Blood. 27(26):3321-3330.
114. Global Manufacturing of CAR T Cell Therapy. Bruce L. Molecular Therapy: Methods & Clinical Development. 2017; 4:92.
115. Commercialization of cellular immunotherapies for cancer. Walker et al. Biochem Soc Trans. 2016; 44(2):329-32.
116. Chimeric antigen receptor-modified T cells in chronic lymphoid leukemia. Porter et al. N Engl J Med. 2011; 365(8):725-733.
117. University of Pennsylvania and Novartis Form Alliance to Expand Use of Personalized T Cell Therapy for Cancer Patients. 2012. Available at: <https://www.pennmedicine.org/news/news-releases/2012/august/university-of-pennsylvania-and>. Accessed Aug 2017.
118. Safety and persistence of adoptively transferred autologous CD19-targeted T cells in patients with relapsed or chemotherapy refractory B-cell leukemias. Brentjens et al. Blood. 2011; 118:4817-4828.
119. T cells with chimeric antigen receptors have potent antitumor effects and can establish memory in patients with advanced leukemia. Kalos et al. Sci Transl Med. 2011; 3(95):95ra73.
120. Chemotherapy-refractory diffuse large B-cell lymphoma and indolent B-cell malignancies can be effectively treated with autologous T cells expressing an anti-CD19 chimeric antigen receptor. Kochenderfer et al. J Clin Oncol. 2015; 33:540-549.
121. Chimeric antigen receptor T cells persist and induce sustained remissions in relapsed refractory chronic lymphocytic leukemia. Porter et al. Sci Transl Med. 2015; 7:303ra139.
122. Randomized, phase II dose optimization study of chimeric antigen receptor (CAR) modified T cells directed against CD19 in patients (pts) with relapsed, refractory (R/R) CLL. Porter et al. J Clin Oncol. 2016; 34: suppl (abstr 3009).

123. Durable Molecular Remissions in Chronic Lymphocytic Leukemia Treated With CD19-Specific Chimeric Antigen Receptor–Modified T Cells After Failure of Ibrutinib. Turtle et al. *J Clin Oncol*. 2017; 35(26):3010-3020.
124. Ibrutinib enhances chimeric antigen receptor T-cell engraftment and efficacy in leukemia. Fraietta et al. *Blood*. 2016; 127(9):1117-1127.
125. CD19 CAR-T cells combined with ibrutinib to induce complete remission in CLL. ASCO Annual Meeting 2017. Gill et al. Available at: http://ascopubs.org/doi/abs/10.1200/JCO.2017.35.15_suppl.7509. Accessed Aug 2017.
126. Novartis next generation CAR-T cell therapy CTL119 combined with ibrutinib shows high rate of responses in CLL patients. 2017. Available at: <https://www.novartis.com/news/media-releases/novartis-next-generation-car-t-cell-therapy-ctl119-combined-ibrutinib-shows-high>. Accessed Aug 2017.
127. Improving Therapy of Chronic Lymphocytic Leukemia (CLL) with Chimeric Antigen Receptor (CAR) T Cells. Fraietta et al. *Semin Oncol*. 2016; 43(2): 291–299.
128. B-cell depletion and remissions of malignancy along with cytokine-associated toxicity in a clinical trial of anti-CD19 chimeric-antigen-receptor transduced T cells. Kochenderfer et al. *Blood*. 2012; 119(12): 2709-2720.
129. Efficacy and toxicity management of 19-28z CAR T cell therapy in B cell acute lymphoblastic leukemia. Davila et al. *Sci Transl Med*. 2014; 6(224):224ra25.
130. Juno Therapeutics' and Celgene Corporation's Investigational Drug JCAR017 Granted Breakthrough Therapy Designation from FDA and Priority Medicines Eligibility from EMA for Relapsed/Refractory Diffuse Large B-cell Lymphoma. 2016. Available at: <http://ir.celgene.com/releasedetail.cfm?releaseid=1005008>. Accessed June 2017.
131. Juno Corporate Presentation. Aug 2017. Available at: <http://ir.junotherapeutics.com/phoenix.zhtml?c=253828&p=irol-presentations>. Accessed Aug 2017.
132. Juno Therapeutics Pipeline. Available at: <https://www.junotherapeutics.com/our-pipeline/>. Accessed Sep 2017.
133. Laboratory Treated T Cells in Treating Patients With Relapsed or Refractory Chronic Lymphocytic Leukemia, Non-Hodgkin Lymphoma, or Acute Lymphoblastic Leukemia. Available at: <https://clinicaltrials.gov/ct2/show/NCT01865617>. Accessed Aug 2017.
134. Anti-CD19 CAR-T cell therapy with defined T-cell subsets for ibrutinib-refractory CLL – presentation at iwCLL 2017. Available at: <http://www.lymphomahub.com/medical-information/anti-cd19-car-t-cell-therapy-with-defined-t-cell-subsets-for-ibrutinib-refractory-cll-presentation-at-iwcll-2017>. Accessed Aug 2017.
135. Targeted antibody-mediated depletion of murine CD19 CAR T cells permanently reverses B cell aplasia. 2016. Paszkiewicz et al. *J Clin Invest*. 2016; 126(11):4262–4272.
136. Juno Therapeutics Announces Complete Response and Corresponding Early Survival Data for JCAR014 in Patients with Ibrutinib-Refractory CLL. Dec 2016. Available at: <http://ir.junotherapeutics.com/phoenix.zhtml?c=253828&p=irol-newsArticle&ID=2227315>. Accessed Aug 2017.
137. CD19 CAR-T Cells Are Highly Effective in Ibrutinib-Refractory Chronic Lymphocytic Leukemia. Turtle et al. Dec 2016. 2016 ASH Annual Meeting. Abstract 56. Presented December 3, 2016. Available at: <http://www.bloodjournal.org/content/128/22/56>. Accessed Sep 2017.
138. Juno Corporate Presentation. Sep 2017. Available at: <http://ir.junotherapeutics.com/phoenix.zhtml?c=253828&p=irol-presentations>. Accessed Sep 2017.
139. A phase I trial of CD19-targeted EGFRt/19-28z/4-1BBL armored chimeric antigen receptor (CAR) modified T cells in patients with relapsed or refractory chronic lymphocytic leukemia. Park et al. *Journal of Clinical Oncology*. 2017; 35(no.15 suppl).
140. A Trial of "Armored" CAR T Cells Targeting CD19 For Patients With Relapsed CLL. Available at: <https://clinicaltrials.gov/ct2/show/record/NCT03085173>. Accessed Aug 2017.
141. Structural Design of Engineered Costimulation Determines Tumor Rejection Kinetics and Persistence of CAR T Cells. Zhao et al. *Cancer Cell*. 2015; 28:415–428.
142. Shifting the Evolving CAR T Cell Platform into Higher Gear. Holohan et al. *Cancer Cell*. 2015; 28:401.
143. Novartis Personalized Cell Therapy CTL019 Receives FDA Breakthrough Therapy Designation. 2014. Available at: <https://www.pharmpro.com/news/2014/07/novartis-personalized-cell-therapy-ctl019-receives-fda-breakthrough-therapy-designation>. Accessed Sep 2017.
144. Novartis announces new CTL019 study data demonstrating overall response in adult patients with certain types of lymphoma. 2015. Available at: <https://www.novartis.com/news/media-releases/novartis-announces-new-ctl019-study-data-demonstrating-overall-response-adult>. Accessed June 2017.
145. Novartis CAR-T cell therapy CTL019 unanimously (10-0) recommended for approval by FDA advisory committee to treat pediatric, young adult r/r B-cell ALL. Available at: <https://www.novartis.com/news/media-releases/novartis-car-t-cell-therapy-ctl019-unanimously-10-0-recommended-approval-fda>. Accessed Jul 2017.
146. FDA approval brings first gene therapy to the United States. Available at: FDA approval. Accessed Aug 2017.

147. Novartis highlights CTL019 data showing its potential in the treatment of specific types of hard-to-treat non-Hodgkin lymphoma. 2015. Available at: <https://www.novartis.com/news/media-releases/novartis-highlights-ctl019-data-showing-its-potential-treatment-specific-types>. Accessed June 2017
148. Novartis announces first CAR-T cell therapy BLA for pediatric and young adult patients with r/r B-cell ALL granted FDA Priority Review. 2017. Available at: <https://www.novartis.com/news/media-releases/novartis-announces-first-car-t-cell-therapy-bla-pediatric-and-young-adult>. Accessed June 2017
149. Novartis CAR-T cell therapy CTL019 receives FDA Breakthrough Therapy designation for treatment of adult patients with r/r DLBCL. 2017. Available at: <https://www.novartis.com/news/media-releases/novartis-car-t-cell-therapy-ctl019-receives-fda-breakthrough-therapy-designation>. Accessed June 2017
150. CTL019 (tisagenlecleucel) In pediatric and young adult patients with relapsed/refractory B-cell acute lymphoblastic leukemia U.S. Food & Drug Administration Oncologic Drugs Advisory Committee Jul 12, 2017. Available at: <https://www.fda.gov/downloads/advisorycommittees/committeesmeetingmaterials/drugs/oncologicdrugsadvisorycommittee/ucm567385.pdf>. Accessed Sep 2017.
151. Novartis' stellar CAR-T efficacy data steamrolls safety doubts to power landmark cancer therapy toward approval. 2017. Available at: <http://www.fiercebiotech.com/biotech/novartis-stellar-car-t-efficacy-data-steamroll-safety-doubts-to-power-landmark-cancer>. Accessed Sep 2017.
152. Novartis CTL019 – JULIET data on DLBCL Investor call. Vas Narasimhan, M.D. Available at: <https://www.novartis.com/sites/www.novartis.com/files/2017-06-ir-call-ctl019-dlbcl-juliet-presentation.pdf>. Accessed Jul 2017.
153. Toxicity and management in CAR T-cell therapy. Bonifant et al. Molecular Therapy Oncolytics. 2016; 3:16011
154. Chimeric Antigen Receptors for T cell Immunotherapy: Current Understanding and Future Direction. Curran et al. J Gene Med. 2012; 14(6): 405–415.
155. Efficacy of Humanized CD19-Targeted Chimeric Antigen Receptor (CAR)-Modified T Cells in Children and Young Adults with Relapsed/Refractory Acute Lymphoblastic Leukemia. Maude et al. 2016; ASH, 58th Annual Meeting and Exposition. Abstract 2017. Available at: <https://ash.confex.com/ash/2016/webprogram/Paper92920.html>. Accessed Aug 2017.
156. Pilot Trial Of Autologous T Cells Engineered To Express Anti-CD19 Chimeric Antigen Receptor (CART19) In Combination With Ibrutinib In Patients With Relapsed Or Refractory CD19+ Chronic Lymphocytic Leukemia (CLL) Or Small Lymphocytic Lymphoma (SLL). Available at: <https://clinicaltrials.gov/ct2/show/study/NCT02640209>. Accessed Aug 2017.
157. Kite Pharma Corporate Website. Available at: www.kitepharma.com. Accessed Jul 2017.
158. Gilead Sciences to Acquire Kite Pharma for \$11.9 Billion. 2017. Available at: <http://www.gilead.com/news/press-releases/2017/8/gilead-sciences-to-acquire-kite-pharma-for-119-billion>. Accessed Aug 2017.
159. Kite Pharma Receives FDA Breakthrough Therapy Designation for KTE-C19 for the Treatment of Refractory, Aggressive Non Hodgkin Lymphoma (NHL). Available at: <http://ir.kitepharma.com/releasedetail.cfm?ReleaseID=945790>. Accessed Jul 2017.
160. Kite Receives U.S. Food and Drug Administration Priority Review for Axicabtagene Ciloleucel. 2017. Available at: <http://ir.kitepharma.com/releasedetail.cfm?ReleaseID=1028075>. Accessed Jul 2017.
161. Kite Files the Industry's First CAR-T Marketing Authorization Application in Europe for Axicabtagene Ciloleucel. Available at: <http://ir.kitepharma.com/releasedetail.cfm?ReleaseID=1035076>. Accessed Sep 2017.
162. Kite corporate presentation. Available at: http://files.shareholder.com/downloads/AMDA-2V2XOY/4859092249x0x945757/29F0F521-5728-4871-AB18-3F8519098BB7/Kite_Corporate_Presentation_-_June_2017.pdf. Accessed Jul 2017.
163. Kite Pharma Details KTE-C19 Launch Preparedness and Near-Term, Next Generation CAR/TCR Product Candidates at Investor Day. 2016. Available at: <http://ir.kitepharma.com/releasedetail.cfm?releaseid=994338>. Accessed Aug 2017.
164. An Assessment of the Number of Chronic Lymphocytic Leukaemia (CLL) Patients Eligible for Front-Line Treatment but Unsuitable for Full-Dose Fludarabine across the European Union. Jeyakumaran et al. Poster presented at the 19th Annual European Congress of the International Society for Pharmacoeconomics and Outcomes Research (ISPOR). 2016. Available at: https://www.ispor.org/research_pdfs/54/pdf/PSY3.pdf. Accessed Aug 2017.
165. Long-term results of first salvage treatment in CLL patients treated initially with FCR (fludarabine, cyclophosphamide, rituximab). Tam et al. Blood. 2014; 124(20): 3059.
166. Follow-Up of RESONATE Trial Supports Survival Benefits of Ibrutinib for Previously Treated CLL. 2017. Available at: <https://am.asco.org/follow-resonate-trial-supports-survival-benefits-ibrutinib-previously-treated-cll>. Accessed Aug 2017.
167. Long-term efficacy and safety with ibrutinib (ibr) in previously treated chronic lymphocytic leukemia (CLL): Up to four years follow-up of the RESONATE study. Byrd et al. ASCO 2017. Available at: <http://meetinglibrary.asco.org/record/147112/abstract>. Accessed Aug 2017.

168. Novartis receives first ever FDA approval for a CAR-T cell therapy, Kymriah™ (tisagenlecleucel, CTL019), for children and young adults with B-cell ALL that is refractory or has relapsed at least twice. 2017. Available at: <https://novartis.gcs-web.com/novartis-receives-fda-approval-for-KymriahTM>. Accessed Sep 2017.
169. How will Novartis price its groundbreaking CAR-T med? R&D exec offers some clues. FiercePharma. June 8th 2017. Available at: <http://www.fiercepharma.com/pharma/novartis-car-t-med-could-rank-among-world-s-costliest>. Accessed Jul 2017.
170. Taking CAR-T cells from first in man trials to marketing authorisation. 2016. Available at: http://www.ema.europa.eu/docs/en_GB/document_library/Presentation/2016/12/WC500217507.pdf. Accessed Sep 2017.
171. Incidence of haematological malignancy by sub-type: a report from the Haematological Malignancy Research Network. Smith et al. Br J Cancer. 2011; 105(11): 1684–1692.
172. Why Most CAR-T Treatments Cannot Be Priced As High As Kymriah. 2017. Available at: <https://seekingalpha.com/article/4105872-gilead-price-car-t-high-kymriah#alt1>. Accessed Sep 2017.
173. Economic Burden of Chronic Lymphocytic Leukemia in the Era of Oral Targeted Therapies in the United States. Chen et al. Clin Oncol. 2017; 35:166-174.
174. Impact of Ibrutinib and Idelalisib on the Pharmaceutical Cost of Treating Chronic Lymphocytic Leukemia at the Individual and Societal Levels. Journal of Oncology Practice. 2015; 11(3): 252-258.
175. Roche/AbbVie team scores 'breakthrough' FDA OK of leukemia drug. 2016. Available at: <http://www.fiercebitech.com/biotech/roche-abbvie-team-scores-breakthrough-fda-ok-leukemia-drug>. Accessed Sep 2017.
176. NHS patients denied access to AbbVie's Venclyxto. 2017. Available at: www.pharmatimes.com/news/nhs_patients_denied_access_to_abbvies_venclyxto_1186848. Accessed Sep 2017.
177. Venetoclax for treating chronic lymphocytic leukaemia. NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE Appraisal consultation document. 2017. Available at: <https://www.nice.org.uk/guidance/gid-ta10077/documents/appraisal-consultation-document-2>. Accessed Sep 2017.
178. The assessment and appraisal of regenerative medicines and cell therapy products: an exploration of methods for review, economic evaluation and appraisal. Hettle et al. 2017. Health Technology Assessment. Volume 21 Issue 7. Available at: <https://www.ncbi.nlm.nih.gov/books/NBK424722/>. Accessed April 2017.
179. The Cost of Hematopoietic Stem Cell Transplantation and Associated Conditioning Regimens. Quock et al. 57th American Society of Hematology Annual Meeting & Exposition December 5–8, 2015. Available at: http://www.pharllc.com/wp-content/uploads/2015/12/HSCT-Poster_FINAL-ASH-2015.pdf. Accessed April 2017
180. Bone Marrow Transplant Cost Guide. Available at: <https://www.medigo.com/blog/medigo-guides/bone-marrow-transplant-cost-guide/>. Accessed Sep 2017.
181. Sipuleucel-T (Provenge) Injection The First Immunotherapy Agent (Vaccine) For Hormone-Refractory Prostate Cancer. Anassi et al. P T. 2011; 36(4): 197–202
182. Amgen slaps record-breaking \$178K price on rare leukemia drug Blincyto. Available at: <http://www.fiercepharma.com/marketing/amgen-slaps-record-breaking-178k-price-on-rare-leukemia-drug-blincyto>. Accessed April 2017.
183. Assessing the Cost–Benefit of Immune Checkpoint Inhibitors. Available at: <http://www.valuebasedcancer.com/issue-archive/2016/september-2016-vol-7-no-8/assessing-the-cost-benefit-of-immune-checkpoint-inhibitors/>. Accessed April 2017.

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