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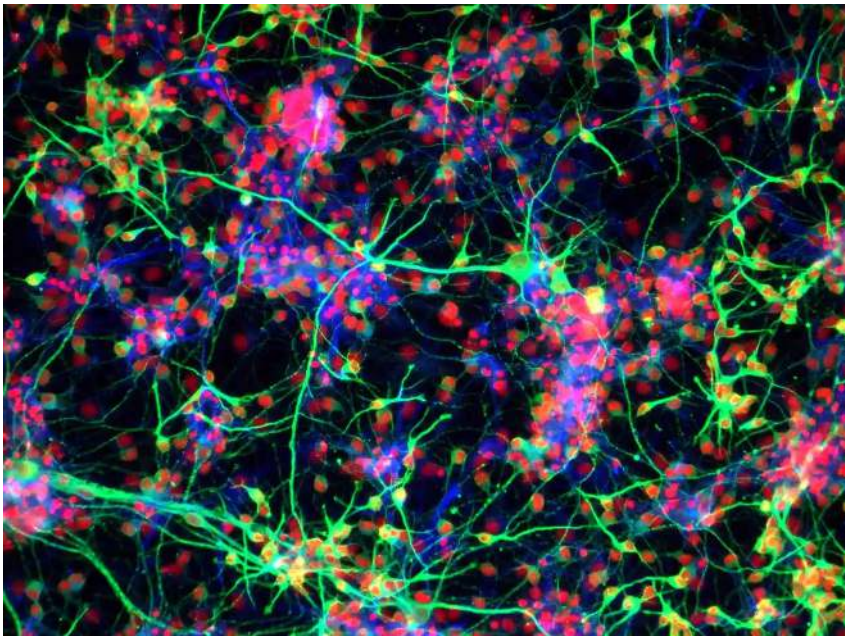
Onco-this-Week

December 8, 2018(https://sciwri.club/archives/date/2018/12/08)



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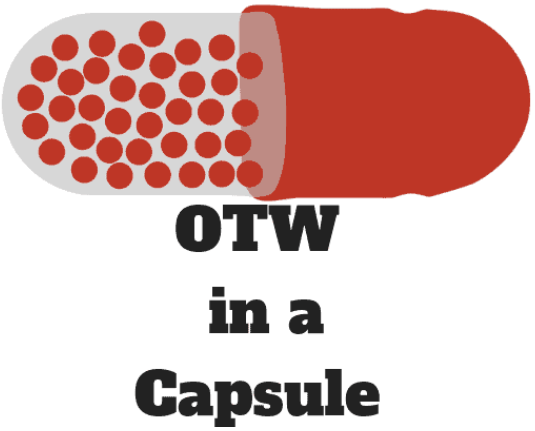
This week's OTW captures more than 50 result updates from 60th ASH Annual Meeting. Read on to find more news updates and our take on implications of approval of Atezolizumab combination therapy in frontline NSCLC patients, priority review to Atezolizumab – chemotherapy combination in ED SCLC, and another setback for Rova-T. The Trivia section contains information on Antibody-drug conjugates, or ADCs.



1. **Approval of Atezolizumab – Bevacizumab – chemotherapy combination in1L EGFR/ALK WT NSCLC patients.** It was a long waitfor Atezolizumab – Bevacizumab – chemotherapy combination in Ph III IMpower150 trial for FDA approval after it showed OS improvement earlier this year in an interim analysis. The PDUFA date given to sBLA was extended by three more months; however, the current approval consolidates Atezolizumab's position in NSCLC since along with frontline, it was also approved in patients with progression during or following platinum-containing chemotherapy, or an appropriate FDA-approved targeted EGFR/ALK inhibitors, in case of EGFR or ALK mutated patients. However, the space is already dominated by Nivolumab and Pembrolizumab, a fact which is going to affect Atezolizumab's sales.
2. **Priority review to Atezolizumab – chemotherapy combination in ED SCLC.** Unlike NSCLC, where the market is dominated by frontrunners Nivolumab and Pembrolizumab, SCLC remains a lucrative space for Ateolizumab. BMS failed to extend Nivolumab's magic in SCLC when it recently failed in maintenance settings and was questioned by analysts for not going for a frontline setting. This fact gives Atezolizumab a space undiluted by the presence of usual rivals, at least for some time. The PDUFA date is set for March 2019 and a approval will be the much-needed boost to Atezolizumab's position in lung cancer, apart from making it the

first frontline approval in last two decades.

3. **Halt on patient enrolment in Ph III TAHOE trial of Rova-T in SCLC.** Rova-T had its first setback earlier this year when it posted poor phaseII TRINITY trial results in heavily pre-treated SCLC patients. The current halt on patient recruitment is a result of observation of independent data monitoring committee, which found patients dying sooner on the Rova-T arm than those on the control arm. It is major setback for DLL3-targeting D6.5 ADC and it would be interesting to see if other Rova-T trials in SCLC (Ph I/II combination trial with nivolumab and ipilimumab in ED SCLC, Ph III MERU trial in1L maintenance settings; and a lower phase trial in solid tumors) succeed or make the opportunities of Rova-T even narrower than how they are right now.

DRUG APPROVALS

Atezolizumab + bevacizumab with chemotherapy combination approved by FDA in 1L EGFR/ALK WT NSCLC based on PhIII IMpower150 trial results (https://www.businesswire.com/news/home/20181206005992/en/FDA-Approves-Genentech's-Tecentriq-Combination-Avastin-Chemotherapy)

"Today's approval supports our combination approach for Tecentriq in lung cancer and our vision to develop medicines that improve outcomes for patients with this complex disease. This Tecentriq regimen has demonstrated a significant survival benefit in the initial treatment of metastatic non-squamous non-small cell lung cancer," said Sandra Horning, M.D., Chief Medical Officer and head of Global Product Development. "Today's approval supports our combination approach for Tecentriq in lung cancer and our vision to develop medicines that improve outcomes for patients with this complex disease."

> The #FDA (https://twitter.com/hashtag/FDA?src=hash&ref_src=twsrc%5Etfw) approved atezolizumab in combination with bevacizumab, paclitaxel, and carboplatin for the first-line treatment of patients with metastatic nonsquamous, NSCLC without EGFR or ALK mutations. https://t.co/3UsiBivn2h (https://t.co/3UsiBivn2h) pic.twitter.com/8D6tiWOGXZ (https://t.co/8D6tiWOGXZ)
>
> — Oncology Newswatch (@OncologyWatch) December 7, 2018 (https://twitter.com/OncologyWatch/status/1071053648275406848?ref_src=twsrc%5Etfw)

https://platform.twitter.com/widgets.js (https://platform.twitter.com/widgets.js)

REGULATORY NEWS

Fate Therapeutics Announces FDA Clearance of Landmark IND for FT500 iPSC-derived, Off-the-Shelf NK Cell Cancer Immunotherapy (https://ir.fatetherapeutics.com/news-releases/news-release-details/fate-therapeutics-announces-fda-clearance-landmark-ind-ft500)

"The clearance by the FDA of our FT500 IND is a significant milestone and marks the beginning of an exciting new era for the clinical development of cell products," said Scott Wolchko, President and Chief Executive Officer of Fate Therapeutics. "Clonal master iPSC lines are a renewable cell source that can uniquely produce cell products which are uniformly engineered and well characterized, can be mass produced in a cost-effective manner, and can be delivered off-the-shelf to treat many patients.This revolutionary paradigm overcomes significant challenges that limit both patient- and donor-derived cell therapy, where heterogeneous populations of primary cells are repeatedly sourced, engineered, expanded and characterized on a batch-by-batch basis resulting in cell therapies with substantial variability in quality, consistency and potency."

> $FATE (https://twitter.com/search?q=%24FATE&src=ctag&ref_src=twsrc%5Etfw) Fate Therapeutics Announces FDA Clearance of IND for FT500 iPSC-derived, Off-the-Shelf NK Cell Cancer Immunotherapy pic.twitter.com/BvdJc2BoW8 (https://t.co/BvdJc2BoW8)
>
> — RVH_Investing_Research (@RVH_VIP) November 30, 2018 (https://twitter.com/RVH_VIP/status/1068498597426225152?ref_src=twsrc%5Etfw)

https://platform.twitter.com/widgets.js (https://platform.twitter.com/widgets.js)

Priority review granted to Atezolizumab + chemotherapy in ED SCLC based on Ph III IMpower133 results; PDUFA: 18th Mar 2019 (https://www.roche.com/media/releases/med-cor-2018-12-05.htm)

"It's been more than 20 years since there has been a new initial treatment option for extensive-stage small cell lung cancer that delivers a clinically meaningful survival benefit," said Sandra Horning, MD, Chief Medical Officer and Head of Global Product Development. "We are working closely with the FDA to bring this Tecentriq-based regimen to people with this difficult-to-treat type of lung cancer as soon as possible."

> In the IMpower133 trial, the addition of atezolizumab to carboplatin and etoposide resulted in significantly longer overall survival than carboplatin and etoposide alone.
>
> — NEJM (@NEJM) December 5, 2018 (https://twitter.com/NEJM/status/1070443950677377024?ref_src=twsrc%5Etfw)

https://platform.twitter.com/widgets.js (https://platform.twitter.com/widgets.js)

TRIAL RESULTS

Ph III KATHERINE trial of adjuvant trastuzumab emtansine met primary endpoint of iDFS reduction in early stage HER2+ breast cancer patients (http://hugin.info/174806/R/2227754/874660.pdf)

"The KATHERINE results demonstrate a significant reduction in the risk of recurrence of HER2-positive early breast cancer in people with residual disease after neoadjuvant therapy, and we look forward to submitting these data to health authorities as soon as possible," said Sandra Horning, MD, Roche's Chief Medical Officer and Head of Global Product Development. "We come closer to the goal of helping each person with early breast cancer have the greatest opportunity for cure with every advance in reducing disease recurrence."

> #Drug (https://twitter.com/hashtag/Drug?src=hash&ref_src=twsrc%5Etfw) Phase III KATHERINE trial crossed early reporting boundary and met its primary endpoint https://t.co/5mBxuGQmv8 (https://t.co/5mBxuGQmv8) pic.twitter.com/NXOlfTDXAo (https://t.co/NXOlfTDXAo)
>
> — PharmaSources.com (@Pharmachina365) December 6, 2018 (https://twitter.com/Pharmachina365/status/1070618917943549954?ref_src=twsrc%5Etfw)

Ph III EAGLE trial of Durvalumab + Tremelimumab failed to meet primary endpoint of OS improvement in recurrent or metastatic SCCHN patients (https://www.astrazeneca.com/content/astraz/media-centre/press-releases/2018/update-on-the-phase-iii-eagle-trial-of-imfinzi-and-tremelimumab-in-advanced-head-and-neck-cancer-07122018.html)

Sean Bohen, Executive Vice President, Global Medicines Development and Chief Medical Officer, said: "The prognosis for recurrent or metastatic head and neck squamous cell cancer is very poor and new treatments for this group of cancers are urgently needed. While these results are disappointing, we remain committed to evaluating the potential of Imfinzi and other innovative medicines for patients with head and neck cancer. We look forward to seeing the results of the Phase III KESTREL trial of Imfinzi and tremelimumab in patients who have not received prior chemotherapy for recurrent or metastatic head and neck squamous cell carcinoma in the first half of 2019."

> Discouraging data for Durva Treme combinations in SCCHN, negative EAGLE trial following CONDOR; @DrNabilSaba (https://twitter.com/DrNabilSaba?ref_src=twsrc%5Etfw) ; EAGLE Trial With Imfinzi & Tremelimumab Fails To Meet Endpoints – https://t.co/E4tgX2vyQc (https://t.co/E4tgX2vyQc) https://t.co/oh7TktspAu (https://t.co/oh7TktspAu)
>
> — Nabil Saba, MD (@DrNabilSaba) December 7, 2018 (https://twitter.com/DrNabilSaba/status/1071149174849191936?ref_src=twsrc%5Etfw)

TRIAL STATUSES

TRIAL STATUS: Ph III TAHOE trial of Rova-T as 2L therapy for advanced SCLC halted (https://news.abbvie.com/news/press-releases/phase-3-trial-rova-t-as-second-line-therapy-for-advanced-small-cell-lung-cancer-tahoe-study-halted.htm)

"Patients are our first priority and we are deeply grateful to the patients and physicians who participated in this trial," said Michael Severino, M.D., executive vice president, research and development and chief scientific officer, AbbVie. "We remain committed to discovering and developing transformative therapies for people living with cancer."

> Unfortunately for Abbvie & for patients, Abbvie terminates TAHOE Phase III trial for Rova-T as second-line therapy fr advanced small-cell #LungCancer (https://twitter.com/hashtag/LungCancer?src=hash&ref_src=twsrc%5Etfw). As we reflect on the $5.6bn acquisition drowning, its a stark reminder of binary risk in drug development https://t.co/Z9NCCZOyKP (https://t.co/Z9NCCZOyKP) pic.twitter.com/EECvill5Hz (https://t.co/EECvill5Hz)
>
> — Pushpa Vijayaraghavan (@pushpa_sathguru) December 6, 2018 (https://twitter.com/pushpa_sathguru/status/1070568537863962624?ref_src=twsrc%5Etfw)

Ph III ASCENT trial of TROP2-targeting SN38 ADC Sacituzumab govitecan started in 3L+ mTNBC patients (https://www.onclive.com/publications/oncology-live/2018/vol-19-no-23/novel-antibodydrug-conjugate-enters-phase-iii-trial-for-metastatic-tnbc?utm_medium=email&utm_campaign=ONCSS%20Breast%20CC%20eNews%20%20Faslodex%20AZ%20%2012-4-18&utm_content=ONCSS%20Breas)

Sacituzumab Govitecan is "like a smart bomb, because the drugs are delivered directly into the tumor. So, with this particular drug, when you attach it to an antibody straight to the tumor, you actually deliver 7-and-a-half times more drug than you'd normally be able to give. That's the reason why we've seen such good results so far," said Linda Vahdat, MD, chief of Medical Oncology and clinical director of Cancer Services at Norwalk Hospital, Connecticut, and a lead investigator in the trial. She also sees patients at Memorial Sloan Kettering Cancer Center in New York.

> Immunomedics Provides Clinical Updates on Breast Cancer Programs With Sacituzumab Govitecan: Updated Phase 2 Results in Metastatic TripleNegative Breast Cancer to be Presented at The 2018 San Antonio Breast Cancer Symposium SABCS Continue to Show... https://t.co/QoIjS8yxOn (https://t.co/QoIjS8yxOn) #cancer (https://twitter.com/hashtag/cancer?src=hash&ref_src=twsrc%5Etfw)
>
> — Cancer News (@Cancer_bio) December 6, 2018 (https://twitter.com/Cancer_bio/status/1070677474382503936?ref_src=twsrc%5Etfw)

"We have worked with this drug for a longtime," said Vahdat. "I was [previously] with the Breast Center at Weill Cornell Medicine and we did all of the baseline work on this drug, not just in breast cancer. We were the first to identify that it was particularly active in TNBC and also in small cell lung cancer and bladder cancer."

Ph III pivotal COSMIC-312 trial of Cabozantinib + Atezolizumab vs Sorafenib initiated in 1L HCC patients (http://ir.exelixis.com/phoenix.zhtml?c=120923&p=irol-newsArticle&ID=2379573)

"Liver cancer is the fastest-rising cause of cancer-related death in the U.S., underscoring the need for new treatment options for this patient community," said Gisela Schwab, M.D., President,Product Development and Medical Affairs and Chief Medical Officer, Exelixis."Based on past evidence of potential synergistic effects with cabozantinib and immune checkpoint inhibitors, the combination offers promise for patients with advanced liver cancer who have not received prior treatment."

"With more than 800,000 new diagnoses of liver cancer worldwide each year and a poor prognosis for patients with advanced disease, there is an urgent need to identify new treatment options," said R.Kate Kelley, M.D., Associate Professor of Clinical Medicine, Division ofHematology/Oncology, University of California, San Francisco, and lead investigator on COSMIC-312. "We look forward to learning whether the combination of cabozantinib and atezolizumab may improve outcomes for previously untreated patients."

First patient dosed in Ph Ib NT-003 trial of Nivolumab + Ipililumab or CD40 agonist APX005M with neoantigen vaccine NEO-PV-01 in metastatic melanoma (https://ir.neontherapeutics.com/news-releases/news-release-details/neon-therapeutics-and-apexigen-announce-first-patient-dosed)

"We believe that there is very strong scientific rationale for treating patients with these additional agents as they may enhance neoantigen immune responses induced by NEO-PV-01 with the potential to drive additional clinical benefit," said Richard Gaynor, M.D., President of Research and Development at Neon Therapeutics.

"CD40 agonists such as APX005M have been shown to enhance antigen presentation, resulting in improved magnitude and quality of T cell responses and we share the enthusiasm of the team at Neon to conduct this clinical trial," said Ovid Trifan, M.D., Ph.D., Chief Medical Officer of Apexigen.

James P. Allison, Ph.D., a Nobel Prize winner, developer of the first FDA-approved checkpoint inhibitor (ipilimumab) and one of Neon's founders, commented, "Both preclinical and clinical work have demonstrated that CTLA-4 antagonism enhances the priming of de novo immune responses and increases T cell infiltration into the tumor. These findings provide clear rationale for combining a checkpoint inhibitor such as ipilimumab with NEO-PV-01 to augment the immune response and potentially transform how we treat cancer."

> CD40 Antibody APX005M, Nivolumab & Chemotherapy Phase 1b 2 Study to Explore Combo Chemotherapy and 2 Immunotherapy Agents https://t.co/99dEfobVMv (https://t.co/99dEfobVMv) pic.twitter.com/3f8JJ5MFKf (https://t.co/3f8JJ5MFKf)
>
> — Oncology Tube (@oncologytube) November 6, 2018 (https://twitter.com/oncologytube/status/1059613709545291777?ref_src=twsrc%5Etfw)

LICENSING DEALS

Cilag GmbH International, an affiliate of Janssen, gets license for anti-CD70 SIMPLE Antibody cusatuzumab (ARGX-110) (https://www.argenx.com/en-GB/news-internal/argenx-enters-exclusive-global-collaboration-and-license-agreement-with-cilag-gmbh-international-an-affiliate-of-janssen-for-cusatuzumab-argx-110/30209/)

"AML continues to be an aggressive and deadly cancer of the blood and bone marrow with very high relapse rates. Cusatuzumab offers a novel mode of action targeting leukemic stem cells, which are a known driver of the relapse mechanism, and has shown a compelling response rate and tolerability profile to date," said TimVan Hauwermeiren, CEO of Argenx. "Janssen is an ideal strategic partner for us to develop this differentiated investigational therapy given its extensive clinical, regulatory and commercial expertise in oncology, and we believe that through this collaboration we are best positioned to reach the broadest number of patients as quickly as possible. The collaboration also strengthens our financial position, enabling our growth into a fully-integrated organization as we continue to exploit our deep pipeline of wholly-owned product candidates, including our lead product candidate efgartigimod which we are evaluating in four severe autoimmune indications."

> Cusatuzumab to be developed for #leukemia (https://twitter.com/hashtag/leukemia?src=hash&ref_src=twsrc%5Etfw), MDS under $1.8B+ collaboration by J&J / @JanssenGlobal (https://twitter.com/JanssenGlobal?ref_src=twsrc%5Etfw)'s Cilag and argenx ($ARGX): https://t.co/XGAATEhZXj (https://t.co/XGAATEhZXj)
>
> — Genetic Engineering & Biotechnology News (@GENbio) December 3, 2018 (https://twitter.com/GENbio/status/1069696542091698178?ref_src=twsrc%5Etfw)

CONFERENCE COVERAGE: 60th American Society Of Hematology (ASH) Annual Meeting

> Welcome, #ASH18 (https://twitter.com/hashtag/ASH18?src=hash&ref_src=twsrc%5Etfw)! SAN has partnered with the @SDConventionCtr (https://twitter.com/SDConventionCtr?ref_src=twsrc%5Etfw) and @ASH_hematology (https://twitter.com/ASH_hematology?ref_src=twsrc%5Etfw) to allow attendees to complete conference registration at the airport from Nov. 29 – Dec. 1. Registration booths are located in T1, T2W, and the International Arrivals Facility. pic.twitter.com/ueaKlC956r (https://t.co/ueaKlC956r)
>
> — San Diego Airport (@SanDiegoAirport) November 29, 2018 (https://twitter.com/SanDiegoAirport/status/1068231783534092288?ref_src=twsrc%5Etfw)

1. Updated data from Ph III MURANO trial of Venetoclax + Rituximab in R/R CLL patients presented (https://news.abbvie.com/news/press-releases/abbvie-presents-new-data-from-phase-3-murano-trial-venclextavenclyxto-venetoclax-in-combination-with-rituximab-in-patients-with-relapsedrefractory-chronic-lymphocytic-leukemia-who-completed-fixed-treatment-course)
2. Brentuximabvedotin + Nivolumab combination data presented in PMBCL and R/R HL patients (http://

investor.seattlegenetics.com/news-releases/news-release-details/seattle-genetics-highlights-multiple-data-sets-evaluating)

3. Updated clinical data from Ph II ZELLA 201 study of CDK9 inhibitor Alvocidib presented in MCL-1 dependent AML patients (https://www.toleropharma.com/our-news/press-releases/press12012018.aspx)
4. Daratumumab combination regimens show positive results for 1L and R/R MM patients in Ph III ALCYONE and Ph II LYRA and GRIFFIN trials (https://www.janssen.com/us/sites/www_janssen_com_usa/files/darzalex_ash_2018_oral_press_release_12.1.18_final.pdf)
5. Positive top-line data from Ph IIb SADAL trial in DLBCL patients presented (https://investors.karyopharm.com/news-releases/news-release-details/karyopharm-reports-positive-top-line-phase-2b-sadal-data)
6. PhI data of anti-BCMA CAR-T bb21217 in RRMM patients presented (http://investor.bluebirdbio.com/news-releases/news-release-details/bluebird-bio-and-celgene-corporation-present-initial-data)
7. Data from Zanubrutinib trials in R/R MCL patients and other heme malignancies presented (http://phx.corporate-ir.net/phoenix.zhtml?c=254246&p=irol-newsArticle&id=2378923)
8. Positive data from anti-CD20 x anti-CD3 bispecific antibody REGN1979 in R/R b-cell NHL presented (https://newsroom.regeneron.com/news-releases/news-release-details/regeneron-presents-positive-data-ash-regn1979-cd20xcd3)
9. Data from REFLECTIONS B328-06 study of Rituximab biosimilar PF-05280586 in FL patients presented (https://www.pfizer.com/news/press-release/press-release-detail/pfizer_presents_positive_26_week_data_for_pf_05280586_a_potential_biosimilar_to_rituximab_at_the_american_society_of_hematology_annual_me
10. PhI/II Liso-cel data in ibrutinib-treated R/R CLL patients, including those with high risk, presented (https://ir.celgene.com/press-releases/press-release-details/2018/Celgene-Corporation-Announces-Initial-Phase-12-Liso-cel-Data-in-Patients-with-RelapsedRefractory-CLL-Including-Those-with-High-Risk-Disease-Previously-Treated-with-Ibrutinib-at-ASH-2018/defau)
11. Updated data from Ph III ECHELON-1 trial of Brentuximab vedotin in 1L advanced HL patients presented (http://investor.seattlegenetics.com/news-releases/news-release-details/seattle-genetics-highlights-additional-analyses-echelon-1-phase)
12. Updated data from Ph III TOURMALINE-MM3 trial of proteasome inhibitor Ixazomib inmultiple myeloma patients in post-transplant maintenance settings presented (https://www.takeda.com/newsroom/newsreleases/2018/takeda-to-present-positive-data-from-tourmaline-mm3-first-pivotal-phase-3-placebo-controlled-trial-evaluating-proteasome-inhibitor-treatment-in-maintenance-setting2/)
13. Updated data from Ph III AUGMENT trial of lenalidmide + rituximab in R/R indolent lymphoma patients presented (https://www.takeda.com/newsroom/newsreleases/2018/takeda-to-present-positive-data-from-tourmaline-mm3-first-pivotal-phase-3-placebo-controlled-trial-evaluating-proteasome-inhibitor-treatment-in-maintenance-setting2/)
14. Updated data from Ph III MEDALIST trial of Luspatercept in patients with very low-,low-, or intermediate-risk non-del(5q) presented (https://ir.celgene.com/press-releases/press-release-details/2018/Celgene-Corporation-and-Acceleron-Pharma-Announce-Results-of-the-Phase-3-MEDALIST-Trial-Evaluating-Luspatercept-in-Patients-with-Myelodysplastic-Syndromes-at-the-ASH-2018-Plenary-Session/defa)
15. Updated results available from pivotal Kymriah (tisagenlecleucel) JULIET and ELIANA trials presented (https://www.novartis.com/news/media-releases/novartis-announces-longer-term-analyses-from-pivotal-kymriah-trials-showed-durable-responses-are-maintained-patients-advanced-blood-cancers)
16. Updated results available from Yescarta (Axicabtagene Ciloleucel) ZUMA-1 trial presented (http://investors.gilead.com/phoenix.zhtml?c=69964&p=irol-newsArticle&ID=2378930)
17. Data from Ph II trial of SY-1425 in AML and MDS patients presented (https://ir.syros.com/press-releases/detail/148/syros-announces-promising-clinical-data-from-ongoing)
18. Data from Ph II trial of Tipifarnib in AITL and PTCL patients presented (http://ir.kuraoncology.com/news-releases/news-release-details/kura-oncology-announces-proof-concept-angioimmunoblastic-t-cell)
19. Updated Ph I data of Indoximod + chemotherapy in 1L AML patients presented (http://investors.linkp.com/news-releases/news-release-details/newlink-genetics-presents-encouraging-updated-phase-1-data)
20. 90% response observed with anti-PD-1 + Umbralisib/Ublituximab in R/R CLL patients in Ph I trial (https://www.onclive.com/conference-coverage/ash-2018/antipd1-plus-umbralisibublituximab-hits-90-response-in-cll?eKey=cnRld2FyaUBzbWFydGFuYWx5c3QuY29t&utm_medium=email&utm_campaign=ONCSS%20GLOBAL%20ASH%20Conference%20Coverage%20eNew
21. Preliminary results from ongoing Ph I ATTCK-17-01 trial of ACTR087 + SEA-BCMA in RRMM patients presented (https://www.nasdaq.com/press-release/unum-therapeutics-presents-preliminary-results-from-ongoing-phase-1-shttps:/www.nasdaq.com/press-release/unum-therapeutics-presents-preliminary-results-from-ongoing-phase-1-study-attck1701-at-the-2018-as-20181201-00030)
22. Promising early data observed with anti-CD3 x anti-CD20 bispecific antibody Mosunetuzumab in NHL patients from Ph I/Ib trial presented (https://www.onclive.com/conference-coverage/ash-2018/mosunetuzumab-shows-promise-for-nonhodgkin-lymphoma?eKey=cnRld2FyaUBzbWFydGFuYWx5c3QuY29t&utm_medium=email&utm_campaign=ONCSS%20GLOBAL%20ASH%20Conference%20Coverage%20eNew
23. High rate of MRD negativity obtained with Ibrutinib/Venetoclax combination in R/RCLL patients (https://www.onclive.com/conference-coverage/ash-2018/ibrutinibvenetoclax-combination-achieves-high-rate-of-mrd-negativity-in-relapsedrefractory-cll?eKey=cnRld2FyaUBzbWFydGFuYWx5c3QuY29t&utm_medium=email&utm_campaign=ONCSS%20GLOBAL%20ASH%20Conference%20Cove)
24. Longer follow-up data of Ibrutinib in CLL patients shows sustained efficacy (Ibrutinib%20Efficacy%20Sustained%20at%207-Year%20Analysis%20for%20CLL)
25. Longer follow-up data of CD79b-targeting ADCPolatuzumab vedotin from Ph Ib/II GO29365 study in R/R DLBCL patients presented (http://hugin.info/174806/R/2227404/874467.pdf)
26. Updated results from Ph I trial of Gilteritiib + chemo in 1L AML patients presented (https://newsroom.astellas.us/2018-12-03-Astellas-Presents-Updated-Results-from-Phase-1-Study-of-Gilteritinib-Plus-Chemotherapy-in-Patients-with-Newly-Diagnosed-Acute-Myeloid-Leukemia-AML)
27. Long term data of Acalabrutinib from Ph II ACE-LY-004 trial in R/R MCL patients andI/II ACE-CL-001 trial in 1L CLL patients confirms efficacy and tolerability (https://www.astrazeneca.com/content/astraz/media-centre/press-releases/2018/new-long-term-data-on-calquence-presented-at-ash-2018-03122018.html)
28. Clinical updates from Tislelizumab in R/R cHL patients in Ph II trial presented (http://phx.corporate-ir.net/phoenix.zhtml?c=254246&p=irol-newsArticle&id=2379122)
29. Updated results from Ph I trial of Ivosidenib in IDH1+ 1L AML patients ineligible for standard treatment and MDS patients presented (http://investor.agios.com/news-releases/news-release-details/agios-presents-updated-data-ivosidenib-phase-1-dose-escalation)
30. PhII interim data from Pracinostat + Azacitidine in high risk MDS patients presented (https://investor.meipharma.com/2018-12-03-Phase-2-Interim-Data-Evaluating-the-Combination-of-Pracinostat-and-Azacitidine-in-Patients-with-Myelodysplastic-Syndrome-Presented-at-the-2018-American-Society-of-Hematology-Annual-Meeting)
31. ME-401data in Ph I trial of patients with indolent B-cell malignancies including R/RFL patients presented (https://investor.meipharma.com/2018-12-02-MEI-Pharma-Presents-Clinical-Data-from-Ongoing-Phase-1b-Study-of-ME-401-in-Patients-with-Indolent-B-Cell-Malignancies-at-the-2018-American-Society-of-Hematology-Annual-Meeting)

32. Selinexor data from Ph IIb STORM trial and Ph Ib/II STOMP trial in RRMM patients presented (https://investors.karyopharm.com/news-releases/news-release-details/karyopharm-reports-updated-selinexor-data-phase-2b-storm-and)
33. Monotherapy and combination therapy data of AFM13 in CD30+ tumors presented (http://www.affimed.com/pdf/20181203_afmd_pr_ash_presentations_fina.pdf)
34. New data with E-selectin inhibitor Uproleselan in 1L and R/R AML patients presented (https://ir.glycomimetics.com/news-releases/news-release-details/glycomimetics-presents-new-aml-data-uproleselan-60th-ash-annual)
35. Clinical data from ongoing Ph I trial of BTKi ARQ 531 in R/R heme malignancies presented (http://investors.arqule.com/news-releases/news-release-details/arqule-announces-clinical-data-ongoing-phase-1-study-reversible)
36. Updated results from Ph II IMerge trial of Imetelstat in low-risk MDS patients presented (http://ir.geron.com/news-releases/news-release-details/geron-reports-updated-results-phase-2-portion-imerge-60th)
37. PhII data of Rigosertib + azacitidine presented in MDS patients (Onconova%20Highlights%20Results%20from%20Phase%202%20Trial%20of%20Oral%20Rigosertib%20In%20Combination%20with%20Azacitidine%20(Vidaz%20in%20Myelodysplastic%20Syndromes%20(MDS)%20at%20the%202018%20ASH%20Annual%20Meeting)
38. NewOS data from IMbark in Imetelstat-treated Int-2 or High-Risk MF and JAK inhibitor- relapsed/refractory patients presented (http://ir.geron.com/news-releases/news-release-details/geron-announces-new-overall-survival-data-imbark-imetelstat)
39. Anti-BCMA CAR-T therapy JCARH125 data presented in RRMM patients (https://ir.celgene.com/press-releases/press-release-details/2018/Celgene-Corporation-Announces-Initial-Clinical-Data-from-Ongoing-Phase-12-Evolve-Trial-with-Anti-BCMA-CAR-T-Therapy-JCARH125-in-RelapsedRefractory-Multiple-Myeloma-at-ASH-2018/default.aspx)
40. PhIII data of Ibrutinib + Obintuzumab in 1L CLL/SLL shows significant PFS improvement (https://news.abbvie.com/news/press-releases/imbruvica-ibrutinib-phase-3-combination-data-with-obinutuzumab-finds-significant-improvement-in-progression-free-survival-pfs-over-standard-chemoimmunotherapy-chlorambucil-plus-obinutuzumab-for-previously-untreat)
41. Updated data from Quizartinib from Ph III QuANTUM-R trial presented; mOS significantly improved (https://www.onclive.com/conference-coverage/ash-2018/quizartinib-update-presented-as-fda-weighs-aml-approval?eKey=cnRld2FyaUBzbWFydGFuYWx5c3QuY29t&utm_medium=email&utm_campaign=ONCSS%20GLOBAL%20ASH%20Conference%20Coverage%20eNew
42. Updated results from Venetoclax studies in CLL (Ph III MURANO) and AML (Ph Ib M14-358and Ph I/II M14-387) presented (http://hugin.info/174806/R/2227619/874569.pdf)
43. PhI results of BiTE Immunotherapies AMG 420 And AMG 330 presented; AMG 420 granted fast track status (https://www.amgen.com/media/news-releases/2018/12/amgen-announces-first-in-human-data-evaluating-investigational-novel-bite-immunotherapies-amg-420-and-amg-330-at-ash-2018/)
44. Updated data from Ph I/II LEGEND-2 trial of BCMA-directed CAR-T cell therapy LCAR-B38M presented in RRMM patients (http://www.legendbiotech.com/gsfiles/ASH_2018_LCAR_B38M_Release_12318_Final.pdf)
45. Updated data from Ph III ECHELON-2 trial of CD30-targeting MMAE ADC, Brentuximabvedotin, in 1L PTCL patients presented (http://investor.seattlegenetics.com/news-releases/news-release-details/seattle-genetics-and-takeda-present-positive-data-phase-3)
46. Updated data from ZUMA-3 trial of KTE-X19 in R/R ALL patients presented (https://www.gilead.com/news/press-releases/2018/12/kite-announces-updated-data-from-zuma3-study-of-ktex19-in-adult-patients-with-relapsed-or-refractory-acute-lymphoblastic-leukemia)
47. Clinical updates from Ph III E1912 trial of Ibrutinib + Rituximab in CLL patients presented (https://www.jnj.com/new-phase-3-study-findings-show-imbruvica-ibrutinib-plus-rituximab-significantly-improved-survival-compared-to-fludarabine-cyclophosphamide-and-rituximab-fcr-in-previously-untreated-patients-aged-70-or-younger-with-chronic-lymphocytic-l)
48. CYAD-01heme malignancies program updated presented (https://www.celyad.com/en/news/celyad-presents-update-on-cyad-01-hematological-malignancies-clinical-program-at-60th-ash-annual-meeting)
49. Data from Ph III MAIA of Daratumumab in 1L MM patients presented (https://www.janssen.com/new-darzalex-daratumumab-phase-3-study-shows-efficacy-and-safety-data-anti-cd38-monoclonal-antibody)
50. Updated data of rituximab biosimilar CT-P10 in FL patients presented (https://www.businesswire.com/news/home/20181204005783/en/)
51. Interim results from ongoing Ph IIa trial of Cerdulatinib in heavily pre-treated T-Cell malignancies presented (http://investors.portola.com/phoenix.zhtml?c=198136&p=irol-newsArticle&ID=2379193)
52. Initial data from Ph I trial of anti-CD123 x anti-CD3 antibody XmAb14045 in R/R AML patients presented (https://investors.xencor.com/news-releases/news-release-details/xencor-presents-initial-data-phase-1-study-xmabr14045-acute)
53. Key outcomes presented from pivotal trial of ELZONRIS in BPDCN, CMML and R/R MF patients (https://ir.stemline.com/news-releases/news-release-details/stemline-therapeutics-recaps-key-clinical-data-presentations)

OTW Trivia

Q: What Are Antibody-Drug Conjugates (ADCs)?

A: ADCs Are Molecules Which Have An Antibody Part (For Targeting A Tumor-Associated Antigen Or TAA) Linked To A Cell-Killing Agent. The Two Parts Are Connected With A Stable Chemical Linker. THE ADC Technology, Thus, Enables Monoclonal Antibodies (MAbs) To Kill Tumor Cells. They Are Specific Owing To The Presence Of TAA-Targeting

MAb And Hence Have Limited Systemic Exposure And Side-Effects.

Q: How Do ADCs Work?

A: The Highly Potent Cytotoxic Anti-Cancer Drug Is Chemically Conjugated To A MAb Using Non-Cleavable Thioether Or Disulfide Linkers That Recognize A Specific Tumor-Associated Antigen – This Design Enhances The Specificity Of The Drug Combination. Once Attached To The Tumor Cells, ADCs Deliver "Deactivated" Cytotoxins To The Cells. Upon Internalization Of The Molecule By Tumor Cell, The Linker Is Degraded, And Cytotoxin Is Released From ADC After Which It Regains Its Full Cytotoxic Activity And Results In Rapid Cell Death Of Tumor Cells, At The Same Time Leaving Normal Cells Unaffected.

Q: What Are Some Examples Of Cytotoxic Drugs Used In ADCs?

A: Some Cytotoxic Drug Classes In Use In ADC Are Inhibitors Of Tubulin Polymerization (E.G., Maytansinoids Or DMs), Dolastatins, Auristatindrug Analogues And Cryptophycin And DNA Alkylating Agents (Esperamicin And Calicheamicin)

Q: What Are Some Examples Of ADCs In Oncology?

A: Some Of The Well-Known ADCs Are CD30-Targeting MMAE ADC Brentuximabvedotin (Https://Adcreview.Com/Brentuximab-Vedotin-Sgn35/),HER2-Targeting DM1 ADC Ado-Trastuzumab Emtansine (Https://Adcreview.Com/Ado-Trastuzumab-Emtansine-Kadcyla-Drug-Description/), CD33-Targeting Calicheamicin ADC Gemtuzumab Ozogamicin (Https://Adcreview.Com/News/Gemtuzumab-Ozogamicin-Granted-Positive-Opinion-Treatment-Previously-Untreated-De-Novo-Cd33-Positive-Aml-Combination-Chemotherapy/), DLL3-Targeting D6.5 ADC Rovalpituzumab Tesirine And CD22-Targeting Calicheamicin ADC Inotuzumab Ozogamicin.

***Source**: https://adcreview.com/adc-university/adcs-101/antibody-drug-conjugates-adcs/*

About the Author:


(https://io.wp.com/www.sciwri.club/wp-content/uploads/2018/03/RT.jpg)

Richa (https://www.linkedin.com/in/richatewari/) earned her PhD at the National Brain Research Centre, India. For her thesis, she worked on the dreaded Glioblastoma multiforme. That was her first in-depth exposure to academic research in cancer biology. After her PhD, she expanded her research experience by working in the field of immunology at UCLA, USA. After her return to India, Richa switched to a corporate setting but continued her engagement with the cancer field. She is currently loving her work, which affords her the opportunity to continue developing her knowledge in the biomedical field of cancer. Outside of work, she enjoys watching, identifying and photographing birds.

Editor and Blog Design:

Abhi Dey (https://www.linkedin.com/in/abhinavdey/)

Abhi graduated from the Molecular Biophysics Unit of IISc (Bangalore, India) in 2011. As a Biomedical Scientist, he has worked with all three life-forms in his 13-year research career, viz., particulate, unicellular and multicellular. He is currently an Assistant Scientist at Emory University (Atlanta, GA) studying mechanisms of tumor recurrence in kids with brain tumors. As a postdoctoral fellow, he was the recipient of two Young Investigator Awards from Alex Lemonade Stand Foundation (Philadelphia, PA) and Rockland Immunochemicals. His current research has been funded by Northwestern Mutual Foundation (Milwaukee, WI), CURE Childhood Cancer Foundation (Atlanta, GA) and American Association for Cancer Research (AACR). When he is not on the bench you will find him spending time with his family or exploring the world through traveling and blogging.

Image Sources: Wikipedia and Twitter

Cover image: "Differentiated rat neural stem cells stained for β III-Tubulin (in green) to reveal neurons, GFAP (in red) to reveal glial cells, and DAPI (in blue) to label nuclei. **Technical Details:** Differentiated rat neural stem cells were fixed andimmunostained β III-tubulin (monoclonal Tuj1 from Stem Cell Technologies), GFAP (from Stem Cell Technologies) and DAPI (from Life Technologies). Images were acquired with SPOT RT Slider CCD camera and SPOT Basic image capture software. Image generated with the Image J color combine function." Source (http://flagella.crbs.ucsd.edu/images/48108)

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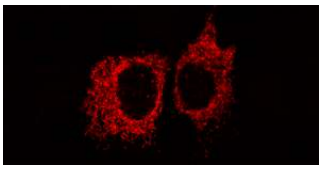

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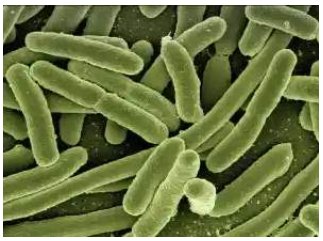

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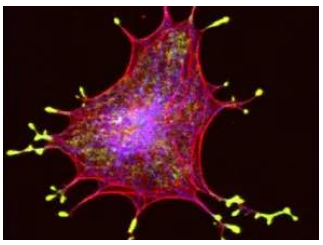

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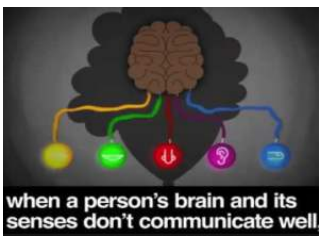

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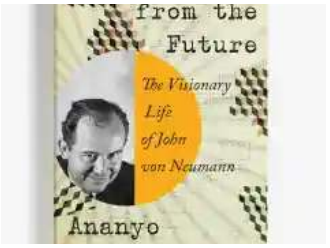

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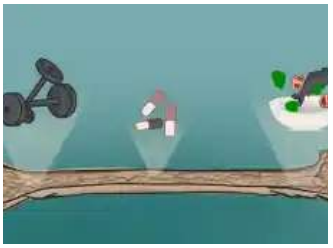

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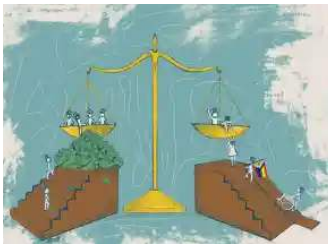

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