Uploaded to the VFC Website

2016

This Document has been provided to you courtesy of Veterans-For-Change!

Feel free to pass to any veteran who might be able to use this information!

For thousands more files like this and hundreds of links to useful information, and hundreds of "Frequently Asked Questions, please go to:

Veterans-For-Change

If Veterans don't help Veterans, who will?

Note: VFC is not liable for source information in this document, it is merely provided as a courtesy to our members & subscribers.

New approaches to treating leukemia, lymphoma and myeloma

Published on December 7, 2015 at 10:46 AM

New, highly targeted treatment approaches for leukemia, lymphoma, and myeloma to be presented today at the 57th American Society of Hematology (ASH) Annual Meeting and Exposition represent a tremendous expansion of oral and intravenous therapy options for patients with blood cancers.

The treatment landscape for hematologic malignancies is evolving rapidly, as recent insights into the genetic signatures of disease continue to inform the development of targeted therapies and identify new uses for those that are already approved. These potent therapies are more effective and potentially safer than standard chemotherapy because they target specific proteins and mutated gene products while leaving other cells unharmed. While these treatments illustrate the exciting progress that researchers have made in the last several years, more options are needed to further improve outcomes for patients.

Studies to be presented today not only illustrate immense progress in the treatment of blood cancers, but they also represent a future of cancer research that is genetically driven and increasingly personalized.

- One presentation will share the results of a promising experimental treatment for acute myeloid leukemia (AML) that targets a specific genetic mutation – the first genetically driven study for a disease for which no new drugs in use have been approved since 1990.
- Another study takes the opposite approach; instead of developing a therapy that hones in on a new target, investigators re-purpose rituximab, a therapy already used to treat a range of cancers of the immune system, to treat B-cell precursor acute lymphocytic leukemia (BCP-ALL), a rare type of leukemia, to improve outcomes in adults who typically respond poorly to treatment.

Two additional studies aimed to identify improved options for patients with relapsed or treatment-resistant multiple myeloma (MM), a cancer of the plasma cells. The two therapies to be presented today, ixazomib and daratumumab, received approval from the United States Food and Drug Administration in November 2015 based on new data.

- One study demonstrates significantly improved response rates by adding ixazomib to standard treatment for patients with relapsed and treatment-resistant multiple myeloma.
- The second MM study offers an entirely new approach to treating this disease with daratumumab, a targeted therapy that represents a significant improvement over the current options for patients.

Finally, three studies report impressive outcomes with new therapies for patients with chronic lymphocytic leukemia (CLL), a blood cancer that occurs when abnormal white blood cells called lymphocytes accumulate in the blood, bone marrow, and lymph nodes or other organs, causing these organs to enlarge. Nearly 70 percent of people affected by CLL are 65 or older:

- A study of ibrutinib, an oral therapy that targets B-cell malignancies, in patients with previously untreated CLL/small lymphocytic lymphoma underscores the promise of targeted therapy for elderly patients.
- A late-breaking study, unblinded early because of "outstanding efficacy," demonstrates that combining orally administered idelalisib with standard treatment for relapsed or treatment-resistant CLL dramatically increases patient survival without disease progression.
- An additional late-breaking study of a high-risk group of CLL patients suggests that venetoclax, an experimental oral therapy improves response rates in a way that has not been seen before in this particular patient population.

"Studies presented today showcase dramatic advances that are revolutionizing the way we treat patients with blood cancers, as well as the promise of novel approaches yet to come," said Gary Schiller, MD, Professor of Medicine in the Division of Hematology/Oncology at the University of California, Los Angeles School of Medicine. "We are seeing how scientific discoveries in the lab are translating into real, positive clinical impact. Patients, especially those with challenging diseases, can be heartened by the tremendous expansion of options and new therapeutic approaches."

This press conference will take place on Sunday, December 6, 2015, at 11:00 a.m. in Room W208AB of the Orange County Convention Center.

First Targeted Therapy for Genetically Defined Subset of Patients with Acute Myeloid Leukemia Significantly Improves Survival

The Multi-Kinase Inhibitor Midostaurin (M) Prolongs Survival Compared with Placebo (P) in Combination with Daunorubicin (D)/Cytarabine (C) Induction (ind), High-Dose C Consolidation (consol), and as Maintenance (maint) Therapy in Newly Diagnosed Acute Myeloid Leukemia (AML) Patients (pts) Age 18-60 with FLT3 Mutations (muts): An International Prospective Randomized (rand) P-Controlled Double-Blind Trial (CALGB 10603/RATIFY [Alliance]) [6]

- Acute myeloid leukemia (AML) is one of the most common forms of adult leukemia. Most of the approximately 30 percent of AML patients whose leukemia cells have a mutation in the *FLT3* gene have a particularly poor prognosis, as their disease tends to be more aggressive and is associated with a higher incidence of relapse. While targeted therapies have improved treatment for other blood cancers, there have been few advances in AML.
- Midostaurin is an experimental drug that inhibits many enzymes, including mutant FLT3.
- This Phase III, multinational, randomized trial analyzed whether adding midostaurin to standard chemotherapy would improve survival when compared to standard chemotherapy alone in adults aged 18 to 60 with this mutation.
- Investigators randomized 717 adult patients with FLT3-mutated AML to receive either midostaurin (360) in pill form or placebo (357) in addition to standard chemotherapy followed by one year of maintenance therapy with the new drug.
- The median time to either failure to achieve remission, relapse, or death in patients who received midostaurin was eight months compared to only three months in the standard treatment arm.
- Standard chemotherapy with midostaurin and one year of maintenance therapy significantly improved median overall survival (74.7 months compared to 26.0 in the group receiving only standard therapy).
- These findings suggest that midostaurin improves outcomes in younger adults with AML with this mutation when added to the standard chemotherapy regimen.

Richard M. Stone, MD, Dana-Farber Cancer Institute, Boston, will present this study during the Plenary Scientific Session on Sunday, December 6, at 2:00 p.m. in Hall D, level 2 of the Orange County Convention Center.

Study Finds New Use for Rituximab in Acute Leukemia

Addition of Rituximab Improves the Outcome of Adult Patients with CD20-Positive, Ph-Negative, B-Cell Precursor Acute Lymphoblastic Leukemia (BCP-ALL): Results of the Randomized Graall-R 2005 Study [1]

- Rituximab is a synthetic molecule engineered to target the protein CD20, which is found on the surface of many blood cancer cells. This therapy is already approved for treating patients with other malignancies, including B-cell non-Hodgkin lymphoma and chronic lymphocytic leukemia.
- CD20 is present in 30 to 50 percent of patients with B-cell precursor acute lymphocytic leukemia (BCP-ALL), a type of leukemia that is common in children but also affects adults. Results of standard therapy in adults is poor compared to results achieved in children.
- This multicenter, randomized clinical trial aimed to evaluate the benefit of adding rituximab to standard chemotherapy for patients aged 18 to 59 with newly diagnosed CD20-positive Philadelphia chromosome-negative BCP-ALL.
- Investigators randomized 220 patients to receive chemotherapy with or without rituximab for a total of 16 to 18 infusions.
- After a median follow up of 30 months, patients who received rituximab had a lower incidence of relapse compared to those who did not (18% in the rituximab arm vs. 30.5% in the control arm). Furthermore, 65 percent of patients in the rituximab arm achieved two-year event-free survival compared to 52 percent of those who did not receive the drug.
- The study suggests that adding rituximab to standard therapy improves event-free survival for patients with BCP-ALL.

Sébastien Maury, MD, Hôpital Henri Mondor, Créteil, France, will present this study during the Plenary Scientific Session on Sunday, December 6, at 2:00 p.m. in Hall D, level 2 of the Orange County Convention Center.

Study Presents Exciting Evidence for First All-Oral Treatment for Relapsed and Treatment-Resistant Multiple Myeloma

Ixazomib, an Investigational Oral Proteasome Inhibitor (PI), in Combination with Lenalidomide and Dexamethasone (IRd), Significantly Extends Progression-Free Survival (PFS) for Patients (Pts) with Relapsed and/or Refractory Multiple Myeloma (RRMM): The Phase III Tourmaline-MM1 Study (NCT01564537) [727]

- One of the current global standards of care for patients with relapsed or treatment-resistant multiple myeloma is a combination of the drug lenalidomide and the steroid dexamethasone. Both of these drugs can be taken in pill form.
- Often a class of drug called proteasome inhibitors can be used in combination with dexamethasone or added to lenalidomide and dexamethasone to improve treatment for relapsed or treatment-resistant multiple myeloma. Until now, proteasome inhibitors have only been available for use intravenously or subcutaneously. Ixazomib is the first of these drugs to be available in pill form. In this Phase III study, 722 patients with relapsed or treatment-resistant multiple myeloma were randomized to receive either the standard treatment regimen of lenalidomide and dexamethasone or a combination of the standard treatment with weekly doses of ixazomib. The median age of patients participating in the trial was 66.
- Patients repeated treatment cycles until their disease progressed or side effects became intolerable.
- At the first interim analysis, the patients who received ixazomib lived a median of 20.6 months without their disease progressing. Patients who received placebo instead of ixazomib demonstrated progression-free survival of 14.7 months.
- Toxicity was similar among both treatment groups, as 68 percent of patients in the ixazomib arm suffered severe but not life-threatening adverse events compared to 61 percent of patients in the placebo group.
- The study suggests that adding ixazomib to standard treatment for relapsed or treatment-resistant multiple myeloma increases time before disease progression. Notably, ixazomib plus lenalidomide and dexamethasone represents the first all-oral combination treatment for multiple myeloma.

Philippe Moreau, MD, University of Nantes, Nantes, France, will present this study during an oral presentation on Monday, December 7, at 2:45 p.m. EST in room Tangerine 2 (WF2), level 2 of the Orange County Convention Center.

First Targeted Therapy for Multiple Myeloma Effective Against Hard-to-Treat Disease

Daratumumab in Combination with Lenalidomide and Dexamethasone in Patients with Relapsed or Relapsed and Refractory Multiple Myeloma (RRMM): Updated Results of a Phase I/II Study (GEN503) [507]

- Myeloma is cancer of the plasma cells, white blood cells that produce infection-fighting antibodies.
- Daratumumab, the first targeted antibody therapy for multiple myeloma, is an experimental agent that is part of a new class of drugs called anti-CD38 antibodies. These drugs first bind to the CD38 protein expressed on the surface of myeloma cells and then signal immune cells to kill the cell directly.
- In this Phase I/II study of daratumumab in combination with standard multiple myeloma therapy, lenalidomide and dexamethasone, researchers sought to evaluate whether this treatment combination is safe and effective for patients with relapsed or treatment-resistant multiple myeloma.
- Thirty-two patients received weekly doses of daratumumab in combination with standard therapy during the first two 28-day therapy cycles and then biweekly infusions during the next four cycles followed by once monthly infusions. Patients received the treatment until their disease progressed or side effects became too severe to continue.
- As of October 2, 2015, 22 patients remained on treatment. Ten (3%) discontinued treatment due to disease progression, adverse events, or investigator decision. The overall response rate was 81 percent and 63 percent had a very good partial response or better.
- The median duration of response was not reached.
- Results of the study suggest that daratumumab is a safe and effective treatment for patients with relapsed or treatment-resistant multiple myeloma.

Torben Plesner, MD, of Vejle Hospital, University of Southern Denmark, Vejle, Denmark, will present this study during an oral presentation on Monday, December 7, at 7:30 a.m. in Hall E1, level 2 of the Orange County Convention Center.

Study Underscores Promise of Targeted Therapies as First-line Approach for Patients with Chronic Lymphocytic Leukemia

Results from the International, Randomized Phase III Study of Ibrutinib Versus Chlorambucil in Patients 65 Years and Older with Treatment-Naïve CLL/SLL (RESONATE™-2) [495]

- Chronic lymphocytic leukemia/small lymphocytic lymphoma (CLL/SLL) primarily affects older patients who often have other chronic diseases or conditions. In this population of patients, chlorambucil has been a standard first-line therapy.
- This randomized, Phase III study sought to evaluate the efficacy and safety of ibrutinib, a first-in-class, oral, Bruton's tyrosine kinase inhibitor that targets B-cell malignancies in newly diagnosed, previously untreated older patients with CLL/SLL.
- Investigators randomized 269 patients with a median age of 73 years to receive either continuous daily doses of ibrutinib or the chemotherapy drug chlorambucil for up to 12 treatment cycles.
- Based on investigator assessment, patients who received ibrutinib achieved an eighteen-month progression-free survival rate of 93.9 percent versus 44.8 percent in patients treated with chlorambucil.
- In addition, patients who received ibrutinib achieved a twenty-four-month overall survival rate of 97.8 percent versus 85.3 percent in patients treated with chlorambucil.
- The results underscore that targeted therapy is effective in patients with previously untreated CLL/SLL and suggest that ibrutinib should be the standard of care for this population.

Alessandra Tedeschi, MD, of Azienda Ospedaliera Niguarda Cà Granda Milano Italy, will present this study during an oral presentation on Monday, December 7, at 7:30 a.m. in room Valencia A (W415A), level 4 of the Orange County Convention Center.

Combination Therapy with Idelalisib Better Prevents Disease Progression in Relapsed or Treatment-Resistant Chronic Lymphocytic Leukemia than Current Regimen

Idelalisib Plus Bendamustine and Rituximab (BR) is Superior to BR Alone in Patients with Relapsed/Refractory Chronic Lymphocytic Leukemia: Results of a Phase III Randomized Double-Blind Placebo-Controlled Study [LBA-5]

- Idelalisib is a targeted therapy which is approved in combination with rituximab for the treatment of patients with relapsed chronic lymphocytic leukemia (CLL). This highly selective compound targets the delta isoform of the PI3 kinase enzyme, which is critical for the activation and survival of CLL cells and other low-grade B-cell lymphomas.
- Researchers conducted a Phase III, randomized, placebo-controlled study that evaluated the efficacy of idelalisib when added to bendamustine and rituximab (BR), the standard treatment regimen for patients with relapsed or treatment-resistant CLL.
- A total of 416 patients were enrolled. Of those, 207 received 150 mg of idelalisib twice daily plus BR, and 209 received placebo plus BR. Patients received six cycles of therapy until their disease progressed or they experienced unacceptable toxicity.
- A pre-specified interim analysis revealed that median progression-free survival, the primary endpoint, was 23 months in the idelalisib arm compared to 11 months in the placebo arm. Based on this result, the Independent Data Monitoring Committee recommended the study be unblinded based on "overwhelming efficacy."
- In addition, there was a statistically significant improvement in overall survival, a secondary endpoint, for patients treated on the idelalisib plus BR arm compared to the BR plus placebo arm.
- The safety profile of idelalisib plus BR was consistent with prior reported studies. The most common severe adverse events were related to low white blood cell count and anemia.
- This study suggests that idelalisib in combination with BR provides better outcomes for patients than BR alone, reducing the risk of both disease progression and death with a tolerable safety provide. This combination is an important new option for patients with relapsed or treatment-resistant CLL.

Andrew D. Zelenetz, MD, PhD, Memorial Sloan Kettering Cancer Center, New York, will present this study during the Late-Breaking Abstracts Session on Tuesday, December 8, at 7:30 a.m. in Hall D, level 2 of the Orange County Convention Center.

Experimental Oral Therapy for Ultra High-Risk Chronic Lymphocytic Leukemia Shows Promise

Venetoclax (ABT-199/GDC-0199) Monotherapy Induces Deep Remissions, Including Complete Remission and Undetectable MRD, in Ultra-High Risk Relapsed/Refractory Chronic Lymphocytic Leukemia with 17p Deletion: Results of the Pivotal International Phase II Study [LBA-6]

- Patients with chronic lymphocytic leukemia (CLL) harboring 17p deletion have a particularly poor prognosis and limited treatment options.
- Venetoclax is an oral, targeted drug that inhibits BCL-2, a protein that regulates natural cell death. BCL-2 is over-expressed in CLL, leading to the accumulation of leukemia cells.
- In a previous Phase I study, venetoclax demonstrated a 77 percent overall response rate for patients with relapsed or treatment-resistant CLL.
- A pivotal Phase II trial was conducted to assess efficacy in CLL patients with 17p deletion. A total of 107 patients with relapsed or treatment-resistant disease took venetoclax once daily with a weekly dose ramp-up schedule. Patients remained on daily 400 mg until disease progression or discontinuation for another reason.
- The primary endpoint was overall response rate as assessed by an independent committee. Efficacy was examined once patients had completed 36 weeks of venetoclax, experienced disease progression, or discontinued the trial.
- The overall response rate was 79.4 percent. Of all responders, 84.7 percent maintained their response at 12 months.
- More than 20 percent of responders had undetectable leukemia cells after therapy.
- More than 10 percent of patients achieved "deep responses" (i.e., no detectable disease or only minimal nodules remaining in the bone marrow), a predictor of long-term remission which has not been previously reported in this population.
- Toxicity was acceptable in this extremely high-risk patient population. Among 11 deaths, seven were due to progressive disease, and four due to adverse events.
- Results suggest that venetoclax is a promising option for this very difficult-to-treat CLL patient population characterized by 17p deletion.

Stephan Stilgenbauer, MD, University of Ulm, Germany, will present this study during the Late-Breaking Abstracts Session on Tuesday, December 8, at 7:30 a.m. in Hall D, level 2 of the Orange County Convention Center.

Source:
American Society of Hematology