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Ibrutinib-venetoclax Demonstrates Clinical Benefits on Undetectable Measurable Residual Disease and Progressive-free Survival in Chronic Lymphocytic Leukemia

Date: September 25, 2025

Chronic lymphocytic leukemia (CLL) refers to a chronic lymphoproliferative disorder, where malignant B cells proliferate and accumulate autonomously via B-cell receptor (BCR) signalling that is mediated by Bruton's tyrosine kinase (BTK). Relevant guideline updates have suggested the use of targeted therapeutic agents over conventional chemoimmunotherapy as first-line treatment for treatment-naïve or refractory CLL. Ibrutinib, an oral BTK inhibitor, blocks BCR signalling and thus reduces CLL-cell proliferation, whereas venetoclax is an oral small-molecule BCL2 inhibitor that induces CLL-cell apoptosis.

The phase 3, multi-centre, randomized and open-label FLAIR trial had recruited a total of 786 eligible patients with untreated CLL. All participants were then randomly assigned in 1:1:1 ratio to receive (1) oral ibrutinib-venetoclax therapy (n=260), (2) oral ibrutinib monotherapy (n=263) or (3) fludarabine-cyclophosphamide-rituximab (FCR) chemoimmunotherapy every 4 weeks for 6 cycles (n=263). Oral ibrutinib was given at a dose up to 420mg daily and the ibrutinib-venetoclax group was also given venetoclax up to 400mg daily for a total of 6 years. The primary endpoints were the undetectable MRD in bone marrow within 2 years after randomization between the oral treatment groups and progression-free survival as compared with the FCR control group.

Undetectable MRD in bone marrow was documented in 66.2% of patients receiving ibrutinib-venetoclax therapy, while all participants in the ibrutinib monotherapy group failed to achieve undetectable MRD within 2 years (P<0.001). With a median follow-up of 62.2 months, disease progression or death occurred in 18 participants (6.9%) in the ibrutinib–venetoclax group, as compared with 59 (22.4%) in the ibrutinib-alone group (hazard ratio=0.29, 95% confidence interval [CI], 0.17-0.49, P<0.001) and 112 (42.6%) in the FCR group (hazard ratio=0.13, 95% confidence interval [CI], 0.08-0.21, P<0.001). No new safety concerns emerged with MRD-guided ibrutinib-venetoclax, with cardiovascular-related adverse effects remain a concern regarding ibrutinib usage.

To summarize, ibrutinib-venetoclax therapy is superior to ibrutinib monotherapy and FCR chemoimmunotherapy with clinical evidence of demonstrating undetectable MRD and extending progression-free survival among patients with chronic lymphocytic leukemia.

Source: www.nejm.org

Trastuzumab Deruxtecan plus Pertuzumab Reduces Progression of Death from HER2-Positive Metastatic Breast Cancer

Date: October 29, 2025

Trastuzumab deruxtecan (T-DXd), an antibody–drug conjugate aimed specifically at HER2, has been effective at treating previously treated HER2-positive metastatic breast cancer, prompting research in patients who are naive to therapy. Pertuzumab combined with trastuzumab and a taxane (THP) is currently an established first-line therapy for HER2-positive advanced or metastatic disease, however it has been unclear whether a T-DXd–based regimen can improve outcomes over THP.

A phase 3, randomized trial enrolled patients with HER2-positive advanced or metastatic breast cancer who had received no prior chemotherapy or HER2-directed therapy for metastatic disease. Participants were randomly assigned in a 1:1:1 ratio to receive T-DXd plus pertuzumab, T-DXd plus pertuzumab-matching placebo, or standard THP (taxane, trastuzumab, and pertuzumab). The primary endpoint was progression-free survival (PFS) by blinded independent central review, while key secondary endpoints included overall survival, objective response, duration of response, safety, and patient-reported outcomes.

At the data-cutoff (February 26, 2025), median progression-free survival was 40.7 months with T-DXd plus pertuzumab and 26.9 months with THP (hazard ratio for progression or death, 0.56; 95% CI, 0.44–0.71; P<0.00001). The confirmed response rate was 85.1% in T-DXd plus pertuzumab versus 78.6% in THP, with complete responses in 15.1% and 8.5%, and median duration of response of 39.2 versus 26.4 months, respectively. However, adjudicated drug-related interstitial lung disease or pneumonitis was more frequent with T-DXd plus pertuzumab (12.1%, including two grade 5 events) than with THP (1.0%, all grade 1–2).

In conclusion, T-DXd plus pertuzumab improves disease control compared to standard THP in HER2-positive metastatic breast cancer, however at the cost of a higher risk of ILD that needs careful monitoring.

Source: www.nejm.org

Amivantamab-Lazertinib Prolongs Overall Survival in EGFR-mutated Advanced Non-small-cell Lung Cancer

Date: October 30, 2025

Non-small-cell lung cancer (NSCLC) is one of the top cancers for new cases and cancer-related deaths in Hong Kong. Various treatment approaches have been approved to target relevant molecular derangements associated with genetic mutations in advanced NSCLC. Although third-generation EGFR-tyrosine kinase inhibitor has been the mainstay of EGFR-mutated advanced NSCLC, drug resistance may become inevitable over time and other clinical alternatives would be required.

The MARIPOSA trial is a phase 3, international, randomized trial comparing the efficacy and safety of amivantamab-lazertinib against osimertinib as first-line therapy in EGFR-mutated advanced NSCLC. A total of 1074 eligible participants were randomized in 2:2:1 ratio to receive (1) amivantamab-lazertinib therapy (n=429), (2) oral osimertinib (n=429) and (3) oral lazertinib (n-216) alone. Patients treated with amivantamab-lazertinib were given weekly amivantamab intravenous infusion for 4 weeks and maintenance infusions every 2 weeks, alongside with oral lazertinib 240mg daily. Overall survival defined as the time from randomization to death from any cause was the key primary endpoint of the current study.

With a median follow-up period of 37.8 months, the amivantamab-lazertinib group was shown to have significantly longer overall survival than conventional osimertinib therapy (hazard ratio for death=0.75, 95% confidence interval [CI], 0.61-0.92, P=0.005). The median time to symptomatic NSCLC progression was also longer in the amivantamab-lazertinib group, as compared with osimertinib alone (hazard ratio=0.69, 95% confidence interval [CI], 0.57-0.83). Yet, the incidence of grade 3 or higher adverse events was more prevalent in amivantamab-lazertinib group (80%) than the osimertinib group (52%).

In conclusion, amivantamab-lazertinib showed clinical significance in prolonging overall survival among EGFR-mutated advanced NSCLC patients as compared with osimertinib.

Source: www.nejm.org

Fish-Oil Supplementation Reduces Rate of Serious Cardiovascular Events in Patients Receiving Hemodialysis

Date: November 7, 2025

Cardiovascular disease is the leading cause of death in patients receiving hemodialysis, yet effective preventive strategies remain limited. Marine n-3 polyunsaturated fatty acids have cardioprotective effects in the general population, but their benefit in dialysis patients has been uncertain.

In a double-blind, randomized, placebo-controlled trial conducted at 26 sites in Canada and Australia (PISCES), adults on maintenance hemodialysis were assigned to receive either fish-oil capsules (4 g/day of n-3 fatty acids, providing 1.6 g EPA and 0.8 g DHA) or a corn-oil placebo. The primary outcome was a composite of serious cardiovascular events, including sudden and non-sudden cardiac death, fatal and nonfatal myocardial infarction, peripheral vascular disease leading to amputation, and fatal or nonfatal stroke. Secondary outcomes were extended from the primary outcome, adding noncardiac death, the individual components of the primary endpoint, and time to the first cardiovascular event or death from any cause.

A total of 1228 participants were randomised, with 610 assigned to fish oil and 618 to placebo, and were followed for a median of 3.5 years. The rate of serious cardiovascular events was significantly lower with fish oil than with placebo (0.31 vs. 0.61 per 1000 patient-days; hazard ratio, 0.57; 95% confidence interval, 0.47 to 0.70; P<0.001). Outcomes like noncardiac deaths, cardiac death, myocardial infarction, amputation, and stroke, and the composite of first cardiovascular event or death from any cause were all reduced with fish-oil supplementation. Meanwhile, adherence and overall adverse event rates were similar in the two groups.

To summarise, these findings show that high-dose fish-oil supplementation significantly lowers serious cardiovascular events in patients receiving hemodialysis than placebo, providing a possible therapy choice for these patients.

Source: www.nejm.org

Evolocumab Lowers Risk of First Cardiovascular Event in Patients without Previous Myocardial Infarction or Stroke

Date: November 8, 2025

Elevated low-density lipoprotein (LDL) cholesterol is yet a major modifiable risk factor for atherosclerotic cardiovascular disease. While statins are the basis of lipid-lowering therapy, the recent development of PCSK9 inhibitors provide an additional choice for intensive LDL reduction. Evolocumab, a monoclonal antibody targeting PCSK9, has demonstrated cardiovascular benefit in secondary prevention, but its role in primary prevention has been less certain.

A recent international, randomized, double-blind, placebo-controlled trial investigated whether evolocumab could reduce the risk of first cardiovascular events in adults without prior myocardial infarction or stroke but at elevated cardiovascular risk. Eligible participants were on optimised lipid-lowering therapy for at least 2 weeks and had LDL cholesterol levels above 2.3 mmol/L, non-HDL cholesterol levels of at least 3.1mmol/L and apolipoprotein B level of at least 80 mg/dL. Participants were assigned to receive either evolocumab (140 mg every two weeks) or placebo, in addition to standard therapy.

The primary outcome was the composite incidence of cardiovascular death, myocardial infarction or stroke (3-point MACE) and a composite of 3-point MACE or ischemia-driven arterial revascularisation (4-point MACE).

A total of 12,257 patients were enrolled (6129 evolocumab, 6128 placebo). The median age was 66 years, and the median follow-up duration was 4.6 years. Evolocumab significantly reduced the risk of 3-point MACE compared with placebo (6.2% vs. 8.0%; hazard ratio [HR], 0.75; 95% confidence interval [CI], 0.65–0.86; P<0.001). For the 4-point MACE, the 5-year Kaplan–Meier estimates were 13.4% with evolocumab and 16.2% with placebo (HR, 0.81; 95% CI, 0.73–0.89; P<0.001).

These findings indicate that evolocumab effectively lowers LDL-C and significantly reduces the risk of a first cardiovascular event in diabetic or atherosclerotic patients without prior myocardial infarction or stroke, reinforcing the role of PCSK9 inhibition in primary prevention for high-risk individuals.

Source: www.nejm.org

Sacituzumab Govitecan Therapy Extends Progression-free Survival in Untreated Advanced Triple-Negative Breast Cancer

Date: November 13, 2025

Triple-negative breast cancer is characterized by the lack of expression of estrogen receptor and progesterone receptor and no overexpression of human epidermal growth factor receptor 2 in tumour cells. Thus, patients diagnosed with triple-negative breast cancer are unlikely to benefit from hormonal therapies with limited treatment options. Sacituzumab govitecan, an antibody-drug conjugate with a potent topoisomerase I inhibitor, targets trophoblast cell-surface antigen 2 (Trop-2) that is highly expressed in triple-negative breast cancer with potential clinical benefits.

In this phase 3, international, open-label and randomized trial, 558 patients diagnosed with untreated advanced triple-negative breast cancer and PD-L1-negtive tumours were assigned in a 1:1 ratio to receive (1) intravenous sacituzumab govitecan at a dose of 10 mg/kg on day 1 & 8 of a 21-day cycle (n=279) or (2) protocol-specified chemotherapy (n=279) as standard of care until disease progression or death. Choices of protocol-specified chemotherapy include paclitaxel albumin or gemcitabine-carboplatin as determined before randomization. The primary endpoint was progression-free survival defined as the time from randomization to disease progression or death from any cause.

As of data-cutoff date in April 2025, the median progression-free survival was 9.7 months with sacituzumab govitecan and 6.9 months with active control (stratified hazard ratio for disease progression or death=0.62, 95% confidence interval [CI], 0.50-0.77, P<0.001). An objective clinical response was also confirmed by blinded central reviewers in 48% of patients receiving sacituzumab govitecan (95% confidence interval [CI], 42-54%) and 46% in the chemotherapy group (395% confidence interval [CI], 40-52%). The incidence rate of grade 3 or above adverse event were similar in both treatment groups.

To summarize, sacituzumab govitecan prolongs progression-free survival in comparison with chemotherapy among patients with advanced triple-negative breast cancer who were not suitable candidates for PD-1 or PD-L1 inhibitors.

Source: www.nejm.org