**LATITUDE: A Phase 3, Double-Blind, Randomized Trial of Androgen Deprivation Therapy With Abiraterone Acetate Plus Prednisone or Placebo In Newly Diagnosed High-Risk Metastatic Hormone-Naïve Prostate Cancer Patients**

- Karim Fizazi, MD, PhD, Head of the Department of Cancer Medicine, Gustave Roussy Cancer Campus, and Professor of Oncology, University Paris-Sud, Villejuif, France

Mortality risk was reduced in the phase 3 LATITUDE trial among men with high-risk, newly diagnosed metastatic prostate cancer when abiraterone acetate (Zytiga, Janssen Biotech) and prednisone were added to androgen deprivation therapy (ADT). While docetaxel plus ADT has been the standard of care for patients with metastatic prostate cancer and high metastatic burden since 2015, abiraterone is much easier to tolerate than docetaxel, Dr. Fizazi said. He noted that patients with newly diagnosed, metastatic, hormone-naive prostate cancer have a poor prognosis, especially in the presence of high-risk characteristics. Among men with newly diagnosed prostate cancer, about 3% in the United States and up to 60% in the Asia-Pacific region have metastatic disease.

LATITUDE included men with two or more high-risk features (Gleason score of 8 or higher, three or more bone lesions, and measurable visceral disease) and randomized them to ADT plus 1,000 mg abiraterone acetate once daily plus prednisone 5 mg once daily (n = 597) or ADT plus placebo (n = 602). The trial, conducted at 235 sites in 34 countries in Europe, Asia-Pacific, Latin America, and Canada, had overall survival (OS) and radiographic progression-free survival (PFS) as its primary efficacy endpoints.

Dr. Fizazi reported that OS was 66% in the group receiving abiraterone and 49% in the placebo group (hazard ratio [HR], 0.62; 95% confidence interval [CI], 0.51–0.76; P < 0.0001). Radiographic PFS was 33.0 months in the abiraterone group and 14.8 months in the placebo group (HR, 0.47; 95% CI, 0.39–0.55; P < 0.0001). Improvements in the secondary endpoints (time to prostate-specific antigen progression, pain progression, next symptomatic skeletal event, chemotherapy, or subsequent prostate cancer therapy) for the abiraterone group were all highly significant.

Grade 3–4 hypertension, hypokalemia, aspartate transaminase increases, alanine transaminase increases, and cardiac disorders were reported more often in the abiraterone group than in the placebo group. These adverse events, Dr. Fizazi noted, were consistent with those reported in prior studies among patients in this population.

“The benefit from early use of abiraterone we saw in this study is at least comparable to the benefit from docetaxel chemotherapy, which was observed in prior clinical trials, but abiraterone is much easier to tolerate, with many patients reporting no side effects at all,” Dr. Fizazi concluded.

ASCO discussant Sumanta Kumar Pal, MD, said: “This is good news because using abiraterone could help many people live longer with fairly few additional side effects.”

**Dacomitinib Versus Gefitinib for the First-Line Treatment of Advanced EGFR-Mutation–Positive Non–Small-Cell Lung Cancer: A Randomized, Open-Label Phase 3 Trial**

- Tony Mok, MD, Professor of Clinical Oncology, Chinese University of Hong Kong, Shatin, Hong Kong

Dacomitinib (Pfizer), an investigational second-generation epidermal growth factor receptor (EGFR) tyrosine kinase inhibitor (TKI), may offer a new option for the management of advanced EGFR-mutated non–small-cell lung cancer (NSCLC). The ARCHER 1050 trial results showed longer progression-free survival (PFS) and duration of response (DOR) for dacomitinib than for gefitinib (Iressa, AstraZeneca), the standard first-generation EGFR TKI. Dr. Mok noted at an ASCO press conference that dacomitinib is characterized by irreversible inhibition of EGFR (also known as human epidermal growth factor receptor 1 or HER1), HER2, and HER4.

The primary endpoint in the open-label phase 3 ARCHER 1050 trial was PFS by blinded independent review. The trial compared oral dacomitinib 45 mg once daily (n = 227) and oral gefitinib 250 mg once daily (n = 225) as first-line treatment for advanced NSCLC with EGFR-activating mutations.

Dr. Mok reported that median PFS was 14.7 months in the dacomitinib arm and 9.2 months in the gefitinib arm (hazard ratio, 0.59; 95% confidence interval, 0.47–0.74; P < 0.0001). PFS rate curves separated quickly at about six months between the two treatment arms, and at 24 months were 30.6% for dacomitinib and 9.6% for gefitinib. While objective responses were
observed for a similar proportion of patients (74.9% for dacomitinib versus 71.6% for gefitinib), median DOR was 14.8 months for dacomitinib and 8.3 months for gefitinib ($P < 0.0001$). Overall survival data, he noted, are not yet mature.

The incidence of adverse events was greater for dacomitinib compared with gefitinib. Dose reduction rates were 66.1% for dacomitinib and 8.0% for gefitinib, with reductions occurring sooner and lasting longer with dacomitinib. With dacomitinib, the most common severe (grade 3) events were acne in 14% of patients and diarrhea in 8% of patients. Liver enzyme abnormalities, the most common severe (grade 3) side effect of gefitinib, were reported in 8% of patients. Dr. Mok commented that dacomitinib shares the issue of increased side effects of the skin and gastrointestinal tract seen with afatinib (Gilotrif, Boehringer Ingelheim), a second-generation agent already approved by the Food and Drug Administration. “In spite of this, the activity seen in this study should allow for consideration of this effective therapy in this patient population,” he said. Dr. Mok concluded that dacomitinib is a more potent EGFR inhibitor.

ASCO expert discussant John Heymach, MD, PhD, commented further: “It’s been nearly 15 years since EGFR-targeted therapies were introduced, helping extend survival for thousands of patients in the time since. The second generation of these therapies is more effective, but can also cause greater side effects, so patients and their doctors will need to weigh the risks and benefits.”

**Phase 3 Trial of Lenvatinib Versus Sorafenib In First-Line Treatment of Patients With Unresectable Hepatocellular Carcinoma**

- Ann-Lii Cheng, MD, Director of the Department of Oncology, and Professor of Internal Medicine, National Taiwan University Hospital, Taipei, Taiwan

In the results of the REFLECT study, lenvatinib (Lenvima, Eisai, Inc.) demonstrated noninferiority for overall survival (OS) versus sorafenib (Nexavar, Bayer HealthCare Pharmaceuticals) for patients with advanced unresectable hepatocellular carcinoma (HCC). Beyond that primary endpoint, lenvatinib was superior to sorafenib in progression-free survival (PFS), time to progression (TTP), and overall response rate (ORR), said Dr. Cheng, the REFLECT lead author, in an oral presentation.

While global phase 3 trials of sunitinib, brivanib (investigational, Bristol-Myers Squibb), linifanib (investigational, Abbott Laboratories), and erlotinib (Tarceva, OSI Pharmaceuticals) plus sorafenib have failed to meet primary endpoints of noninferiority or superiority over the past 10 years in HCC, sorafenib has been the only first-line systemic drug to extend OS. Lenvatinib, an oral multikinase inhibitor, targets vascular endothelial growth factor receptors 1, 2, and 3, fibroblast growth factor receptors 1, 2, 3, and 4, platelet-derived growth factor alpha, and RET and KIT oncogene mutations. Lenvatinib is currently approved for use in thyroid cancer and renal cell carcinoma in the United States. It has shown promising clinical activity in prior phase 2 research among advanced HCC patients.

REFLECT investigators enrolled 954 uHCC patients (mean age, 61 years; 85% male), randomizing them 1:1 to lenvatinib dosed according to body weight (60 kg or greater, 12 mg per day; less than 60 kg, 8 mg per day) or sorafenib 400 mg (twice daily). All patients had one or more measurable target lesions, Barcelona Clinic liver cancer stage B or C, Child–Pugh class A liver disease, Eastern Cooperative Oncology Group performance status of 1 or less, and no prior systemic therapy. OS was the primary endpoint.

Although results were not adjusted for duration of treatment, Dr. Cheng reported that median duration of treatment was 5.7 months in the lenvatinib group and 3.7 months in the sorafenib group, with 87.6% and 83.0% of the planned starting doses being delivered in the lenvatinib and sorafenib groups, respectively.

Median OS was similar for the two groups: 13.6 months in the lenvatinib group (95% confidence interval [CI], 12.1–14.9) and 12.3 months in the sorafenib group (95% CI, 10.4–13.9) (overall hazard ratio [HR], 0.92; overall 95% CI, 0.79–1.06). The noninferiority standard had been set at an HR of less than 1.08.

These results were “well below the noninferiority margin. Therefore, lenvatinib met its primary endpoint of noninferiority to sorafenib,” Dr. Cheng said. OS trends favored lenvatinib across all subgroups with the exception of neutral findings in the Western population (non-Asia–Pacific) and those with macrovascular invasion or extrahepatic spread.

PFS by modified RECIST criteria, a secondary endpoint, also favored lenvatinib at 7.4 months versus 3.7 months for sorafenib (HR, 0.66; $P < 0.00001$). PFS was extended with lenvatinib in all subgroups. TTP estimates favored lenvatinib similarly at 8.9 months versus 3.7 months for sorafenib (HR, 0.63; $P < 0.00001$).

Among additional secondary endpoints, the ORR (complete plus partial responses) for lenvatinib was 24.1% versus 9.2% for sorafenib (odds ratio, 3.13; 95% CI, 2.15–4.56; $P < 0.00001$). Progressive disease rates were 14.9% for lenvatinib and 30.9% for sorafenib, and disease control rates (complete plus partial response plus stable disease) were 75.5% for lenvatinib and 60.5% for sorafenib.

Dr. Cheng noted that higher levels of baseline alpha-fetoprotein (AFP) are associated with poor outcomes in HCC patients. A REFLECT analysis stratified according to AFP levels of less than 200 ng/mL or 200 ng/mL or greater confirmed that higher levels of AFP were associated with less favorable outcomes. In the patients with higher baseline AFP, median OS was 10.4 months for lenvatinib compared with 8.2 months for sorafenib (HR, 0.78).

Dose modification, reduction, or interruption rates for treatment-emergent adverse events were similar for lenvatinib and sorafenib. Serious adverse event rates, however, were higher for lenvatinib (18% versus 10%). Grade 3–4 hypertension was reported at a rate of 23% in the lenvatinib group and at 14% in the sorafenib group. Grade 3–4 skin problems (such as palmar–plantar erythrodyssesthesia) were more common in the sorafenib group (3% for lenvatinib versus 11% for sorafenib).

Assessment of health-related quality of life (QOL) as measured through the most recent European Organization for Cancer Research and Treatment (EORTC) QOL Core Questionnaire C30 and the EORTC Liver Cancer Module (QLQ-HCC12) showed similar results for patients treated with lenvatinib or sorafenib.
The investigator-initiated, open-label, phase 3 SIRveNIB study compared selective internal radiation therapy (SIRT) versus sorafenib (Nexavar, Bayer HealthCare Pharmaceuticals, Inc.) in patients with locally advanced hepatocellular carcinoma (HCC). SIRT with SIR-Spheres yttrium-90 (Y-90) resin microspheres (Sirtex Medical, Inc.) is approved for the treatment of colorectal hepatic metastases and entails a one-time delivery of the microspheres to the liver via the hepatic artery. Sorafenib, an approved oral molecular targeted therapy that requires continuous oral dosing at 400 mg twice daily, was administered in this trial for a median of 13.8 weeks.

Dr. Chow noted that the majority of patients with HCC have locally advanced disease with or without portal vein thrombosis at diagnosis. Those included in the SIRveNIB trial had disease that was not amenable to curative therapies (surgery or transplantation) and had Asian Barcelona Clinic liver cancer stage B and C without extrahepatic metastasis.

“The SIRveNIB rationale was that a definitive phase 3, randomized, controlled trial comparing these two promising therapies in locally advanced HCC would impact on outcomes in a large number of patients and potentially change clinical practice,” Dr. Chow said. The SIRveNIB primary endpoint was overall survival (OS).

SIRveNIB investigators assigned 182 patients to SIRT and 178 to sorafenib. The patients were treated in 27 centers in 11 countries. Mean age overall was approximately 60 years, and about 83% of the patients were men. Fifty-two patients (28.6%) among those randomized to SIRT did not receive the allocated therapy, mostly because of anatomic ineligibility, and 16 patients in the sorafenib group (8.9%) did not receive the allocated therapy.

In the primary intention-to-treat (ITT) analysis, median OS in the SIRT and sorafenib arms was similar at 8.84 months and 10.02 months, respectively (hazard ratio [HR], 1.12; \( P = 0.360 \)). In the treated population, median OS was 11.27 months for SIRT and 10.41 months for sorafenib (HR, 0.86; \( P = 0.273 \)). Among secondary endpoints in the ITT population, tumor response rates (TRR) were 16.5% for SIRT and 1.7% for sorafenib (\( P < 0.001 \)).

For some patients, down-staging of the tumor from “locally advanced” to identical to an “early cancer” after SIRT treatment can be consequential. Tumors once assessed as inoperable become surgery-eligible, and transplantation may also open up as an option. Outcomes for this category of SIRT patients, who are being tested in a subsequent, separate study at 16 centers, are identical to those of patients whose tumors are initially of similar size. “So for this small proportion of patients, this strategy is potentially curative,” Dr. Chow commented. In his surgical center, about 10% of SIRveNIB patients had tumors that were down-staged.

In other ITT secondary endpoints, time to tumor progression (TTP) was 6.08 months for SIRT versus 5.36 months for sorafenib overall (HR, 0.88; \( P = 0.287 \)) and 6.11 months for SIRT versus 5.39 months for sorafenib for liver progression specifically (HR, 0.87; \( P = 0.241 \)). Median progression-free survival (PFS) was 5.85 months for SIRT versus 5.06 months for sorafenib overall (HR, 0.89; \( P = 0.306 \)) and 6.01 months for SIRT versus 5.06 months for sorafenib for liver progression specifically (HR, 0.88; \( P = 0.259 \)). Advantages for SIRT in the treated population, however, were significant for median TTP overall (\( P = 0.019 \)), median TTP in the liver (\( P = 0.013 \)), median PFS overall (\( P = 0.013 \)), and median PFS in the liver (\( P = 0.009 \)).

Adverse event rates were significantly lower in the SIRT arm. “For clinicians and patients, this is very important,” Dr. Chow said. Sixty percent of SIRT patients and 84.6% of sorafenib patients had at least one adverse event (\( P < 0.001 \)). Treatment-related adverse events were reported in 31.5% of SIRT patients and in 74.7% of sorafenib patients (\( P < 0.0001 \)). Treatment-related grade 3 or higher events occurred in 27.7% of SIRT patients and in 50.6% of sorafenib patients (\( P < 0.0001 \)). The adverse events occurring significantly more often in the sorafenib arm were diarrhea (\( P < 0.001 \)), alopecia (\( P < 0.0001 \)), palmar-plantar erythrodysesthesia (\( P < 0.0001 \)), rash (\( P < 0.0001 \)), and hypertension (\( P < 0.0001 \)).

“Although the study is negative for the superiority primary endpoint ... one therapy is clearly less toxic for the patient,” Dr. Chow noted further that SIRT group patients had significantly better TRR, TTP and PFS. “SIRveNIB results can help clinicians and patients make informed treatment choices,” he concluded.
**Meeting Highlights: European League Against Rheumatism**

**European League Against Rheumatism**
The annual European Congress of Rheumatology of the European League Against Rheumatism (EULAR 2017) hosted more than 14,300 attendees from 130 different countries in Madrid from June 14–17. We review below sessions on rheumatoid arthritis and axial spondyloarthritis.

**Little to No Placental Transfer of Certolizumab Pegol During Pregnancy: Results From CRIB, A Prospective, Post-Marketing, Multicenter Pharmacokinetic Study**
• Xavier Mariette, MD, PhD, Head of Rheumatology, Bicêtre Hospital, University Paris-Sud, Paris, France

Transfer of certolizumab pegol (Cimzia, UCB) across the placenta during the third trimester was absent or minimal in the CRIB trial, which was conducted in pregnant women remaining on active treatment for rheumatoid arthritis (RA).

Chronic inflammatory diseases, such as RA, often affect women of reproductive age. Because high disease activity is associated with increased risk of adverse pregnancy outcomes, adequate disease control is crucial, Dr. Mariette said. While RA activity improves spontaneously during pregnancy in some women, about half still need effective therapeutic intervention.

“Tumor necrosis factor [TNF] inhibitors represent one of the most significant advances in the treatment of inflammatory diseases like rheumatoid arthritis, psoriatic arthritis, and axial spondyloarthritis/ankylosing spondylitis [axSpA/AS], but research suggests that most of these drugs cross the placenta, so they are usually discontinued during pregnancy,” he said.

The molecular structure of certolizumab pegol, however, should prevent placental transfer because it does not contain a fragment crystallizable (Fc) region. The Fc receptor is a protein associated with immune function found on some cell surfaces.

Using a highly sensitive and previously validated enzyme-linked immunosorbent assay with anti-certolizumab pegol antibody levels greater than 2.4 units/mL defined as positive, CRIB investigators assessed 16 women who were pregnant for 30 weeks or longer. The women decided to continue on or to start treatment with certolizumab pegol for an approved indication with their treating physician prior to participation in the trial. Blood samples were collected from the mothers and umbilical cords, and were also collected from the infants at delivery and again four and eight weeks after delivery. The CRIB primary analysis was of infant certolizumab pegol levels at birth. Secondary analyses were of mother and umbilical cord blood samples.

The mean age of the mothers was 31 years (range, 18–41 years). Eleven of them had RA, three had Crohn’s disease, one had psoriatic arthritis, and one had axSpA/AS. Mean infant birth weight was 3.3 kg.

Dr. Mariette reported that maternal certolizumab pegol plasma levels at delivery were within the expected therapeutic range (median, 24.4 mcg/mL; range, 5.0–49.4 mcg/mL). Samples were evaluable from 14 of the 16 infants delivered, and among these 14 infants, 13 had no quantifiable certolizumab pegol levels at birth (less than 0.032 mcg/mL). One infant whose mother had a certolizumab pegol level of 49.4 mcg/mL had a minimal level of 0.042 mcg/mL (infant/mother plasma ratio, 0.09%). At weeks 4 and 8, none of the infants had quantifiable levels of certolizumab pegol.

Levels of certolizumab pegol were quantifiable in three of 15 umbilical cord samples (maximum, 0.048 mcg/mL). The maximum cord/mother plasma ratio for these three cords was 0.0023. No anti-certolizumab pegol antibodies were detected in the mothers, umbilical cords, or infants.

Adverse events experienced by the infants did not show any patterns or clusters of events suggesting a specific safety signal in children. Their safety profiles were consistent with those of unexposed similar-age infants. Safety data in the mothers were in line with the known safety profile of certolizumab pegol.

Dr. Mariette concluded that the CRIB study “shows minimal to no placental transfer from mother to infant. This is very encouraging news for female patients who have an active inflammatory disease.” He added, “CRIB results support continuation of certolizumab pegol treatment during the third trimester of pregnancy if anti-TNF therapy is considered necessary.”

**Four-Year Imaging Results Demonstrate Low Disease Progression and Long-Term Efficacy of Certolizumab Pegol in Patients With Axial Spondyloarthritis**
• Désirée van der Heijde, MD, PhD, Professor of Rheumatology, Leiden University Medical Center, Leiden, The Netherlands

In the first report of long-term imaging results for anti-tumor necrosis factor (TNF) treatment of patients with axial spondyloarthritis (axSpA), reductions in inflammation of the spine and sacroiliac joints were maintained with continuous certolizumab pegol treatment over four years.

“Objective information from imaging is important,” Dr. van der Heijde noted in an interview, “because, especially in axial spondyloarthritis, many of the outcome measures are purely patient reported, and few abnormalities can be found by physical investigation. The imaging data complete the clinical data, which by themselves do not give a full picture.” Magnetic resonance imaging (MRI) reveals objective signs of inflammation, and radiographs show structural damage, she explained.

Dr. van der Heijde’s imaging analysis was subsequent to an earlier presentation of data from the RAPID-axSpA trial, a phase 3, multicenter, randomized, double-blind, placebo-controlled study of certolizumab pegol in patients with axSpA, ankylosing spondylitis (AS), and nonradiographic axSpA (nr-axSpA). That study had shown rapid clinical improvements after 12 weeks of treatment that were then sustained through four years of treatment in patients with both AS and nr-axSpA. MRI and spinal x-rays at 96 weeks had shown evidence, respectively, of reduced inflammation and limited progression.

The current study objective was to report both x-ray and MRI assessments over four years of certolizumab pegol treatment in a population of 315 axSpA patients (mean age, 39.7 years). The treated population, Dr. van der Heijde said in her oral...
presentation, included patients with AS and nr-axSpA. MRI assessments were available for 158 patients, and 198 had one or more modified Stoke Ankylosing Spondylitis Spinal Score (mSASSS) assessments. In addition, 273 patients had sacroiliac joint x-rays at baseline. Mean patient age was 41.5 years for those with AS (n = 174) and 37.5 years for those with nr-axSpA (n = 141).

Spinal progression over four years of treatment with certolizumab pegol in both AS (n = 113) and nr-axSpA (n = 83) patients was limited, Dr. van der Heijde reported. From baseline to 96 weeks, mSASSS scores increased in AS patients by 0.67 from 13.17 to 13.84, and at week 204 had increased by only 0.31 to 14.16 (an overall increase of 0.98 for weeks 0–204). The mSASSS scores in nr-axSpA patients decreased by 0.01 from 4.42 to 4.41 at week 96, and increased by 0.07 to 4.47 at week 204 (an overall increase of 0.05 for weeks 0–204).

Progression from nr-axSpA to AS over four years occurred in 4.5% of patients (n = 42). Over the same period, 4.3% (n = 89) improved from AS to nr-axSpA.

The percentage of AS patients in spinal remission (defined as a Berlin spine score of 2 or less) increased from 42.4% at baseline to 67.2%, 67.6%, and 76.0% at weeks 12, 96, and 204, respectively. The percentage of nr-axSpA patients in spinal remission increased from 62.3% at baseline to 76.2%, 69.6%, and 84.4% at weeks 12, 96, and 204, respectively. The percentage of patients in sacroiliac joint remission (defined as a Spondyloarthritis Research Consortium of Canada [SPARCC] score of less than 2) increased from 52.7% at baseline to 85.7%, 83.6%, and 75.6% at weeks 12, 96, and 204, respectively, for those with AS, and increased from 43.3% at baseline to 69.8%, 72.3%, and 80.6% for nr-axSpA patients at the same respective time points.

MRI improvements in Berlin spine score were sustained in both AS and nr-axSpA patients. The mean baseline score of 7.4 in AS patients decreased to 2.7, 2.7, and 2.6 at weeks 12, 96, and 204, respectively. In nr-axSpA patients, it decreased from 4.2 to 1.4, 1.6, and 1.4 at weeks 12, 96, and 204, respectively. Similarly, MRI assessments of SPARCC sacroiliac joint score revealed sustained improvements, with the baseline score of 8.5 in AS patients decreasing to 2.0, 1.3, and 1.8 at weeks 12, 96, and 204, respectively. In nr-axSpA patients, scores also decreased from a baseline of 7.7 to 2.3, 2.5, and 2.0 at weeks 12, 96, and 204, respectively.

“These imaging data confirm the good clinical outcome over four years during treatment with certolizumab,” Dr. van der Heijde concluded.

High Multibiomarker Disease Activity Score Is Associated With High Risk of Radiographic Progression in Six Studies

- Eric H. Sasso, MD, Vice President, Medical and Scientific Affairs, Crescendo Bioscience, Inc., South San Francisco, California

An analysis of six study cohorts that included more than 800 rheumatoid arthritis (RA) patients shows a strong correlation between the score on Vectra DA (12-biomarker blood test, Crescendo Bioscience, Inc.) and the risk of radiographic progression (RP). Included patients had received conventional disease-modifying antirheumatic drugs alone or with adalimumab, infliximab, or abatacept (Orencia, Bristol-Myers Squibb) for one year.

Joint inflammation and damage are important determinants of disability in patients with RA, Dr. Sasso noted. Vectra DA, a multibiomarker disease activity (MBDA) test, analyzes 12 serum protein biomarkers and uses a validated algorithm to generate a single score that represents the level of RA disease activity. RA disease activity is rated on a scale of 1 to 100 with categories of low (less than 30), moderate (30–44), and high (greater than 44). The Vectra DA assay has been tested and validated in more than 3,000 patients, Dr. Sasso said. The test is not currently approved by the Food and Drug Administration.

While MBDA scores have been shown previously to correlate with risk for RP in RA, the current meta-analysis of one registry (Leiden) and five randomized controlled trials (OPERA, SWEFOT [year 1], SWEFOT [year 2], AMPLE [year 1], and AMPLE [year 2]), each with more than 100 RA patients, was performed to more strongly establish this correlation. RP was defined via the threshold for change in modified total Sharp score (ΔmTSS) specific to each study (i.e., 2 to greater than 5 mTSS units per year).

Positive predictive value (PPV) and negative predictive value (NPV) were determined for each study by comparing patients in a high MBDA category with those in a low/moderate category. The high disease activity category was defined by the parent study’s criteria, which included an MBDA score greater than 44; disease activity score 28-joint count C-reactive protein (DAS28-CRP) greater than 4.09 or greater than 5.1; and CRP greater than 3.0 mg/dL.

Dr. Sasso reported at his poster that in each of the six studies, there was a strong relationship between high Vectra DA scores (greater than 44) and RP relative risk (RR) (range, 3.6–9.5). The superior predictive value of Vectra DA was underscored, Dr. Sasso said, by the meta-analysis of the Leiden, SWEFOT Year 1, and OPERA Year 1 studies. Patients with a high Vectra DA score were 5.1 times more likely to develop RP than those with low Vectra DA scores. In comparison, patients were 1.4 times more likely to develop RP than patients with risk assessed by DAS28-CRP (P = 0.23) and 1.6 times more likely than those measured by CRP alone (P = 0.01).

PPV for an MBDA score greater than 44 ranged from 18% to 31%, and the NPV ranged from 93% to 97% (RR, 3.6–9.5), which was considered highly significant. “Based on high NPVs (93% or greater), the MBDA score used alone has clinical value for identifying patients with little or no risk of radiographic progression,” Dr. Sasso said.

“We believe combining the Vectra DA score with conventional clinical measures will enable physicians to individualize treatment plans for their patients, improve outcomes, and reduce the burden of future health care costs associated with this disabling disease,” he concluded.