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Novartis' Bouchard On Delivering Personalized Cancer Medicine In Asia Pacific, Middle East, Africa

by Anju Ghangurde

Francis Bouchard, Region Head for AMACO (Asia Pacific, Middle East and Africa Countries), Novartis Oncology, discusses a range of issues around mainstreaming personalized/precision oncology therapies such as Kymriah in the region, including reimbursement systems, partnerships and digital initiatives.

Overseeing *Novartis AG*'s oncology business across the AMACO (Asia Pacific, Middle East and Africa Countries) region, which comes with strikingly diverse healthcare systems, is likely highly demanding even in normal times, especially as new individualized treatments such as Kymriah (tisagenlecleucel) require sophisticated manufacturing and supply chain processes alongside navigating complex pricing and access issues.

Cut to the early pandemic period and the "difficulty level," if one were to borrow gaming jargon, simply skyrocketed almost overnight across multiple operational aspects, disrupting oncology treatment pathways significantly.

Pre-pandemic cancer diagnosis and treatment gaps in the region widened, with the cracks in fragile healthcare systems in some countries under intense pressure and translating into a dramatic increase in missed diagnoses.

Are there region-specific R&D initiatives being pursued by Novartis given the alarming statistics in areas like lung, breast, and stomach cancers in Asia?

Bouchard: Over 70% of the world's population lives in our region and over half of cancer incidences are from this region. There are certain types of cancers more prevalent here, such as pre-menopausal breast cancer, EGFR-

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In a wide-ranging interview with *Scrip*, Francis Bouchard, Region Head for AMACO, Novartis Oncology, discussed how the Swiss multinational continued to deliver life-saving treatments amid the raging pandemic, even going through with the registration and treatment roll-out of its chimeric antigen receptor T-cell (CAR-T) therapy Kymriah in Saudi Arabia amid all the turbulence.

He also outlined how the Swiss group is pressing ahead with preclinical and translational research project collaborations with different academic centers across Asia. *(See Side Box.)*

"Collaboration and purpose-driven commitment go hand-in-hand to make patient access possible, and the pandemic was a true test of this as it put us through one of the toughest challenges I have encountered in my 30 years at Novartis," Bouchard told *Scrip*.

Critical measures taken to ensure Kymriah reached those who needed it ranged from continuously and closely monitoring the supply chain to putting in place alternative logistical routes for CAR-T therapies, including using cargo flights to transport these treatments instead of passenger flights previously.

"This has meant that our manufacturing facilities have remained operational for commercial and clinical trial patients since the start of the pandemic," Bouchard explained.

Broadly put, the process for producing the

mutated lung cancer, liver cancer, gastric cancer and nasopharyngeal cancer. In order to deliver on rising patient needs, we have globally-integrated programs and world class cancer centers that are regionally led.

Our R&D Center in Shanghai [China] is part of our global program and is one of the key R&D sites for Novartis globally, drawing on our global knowledge and resources to develop innovative cancer treatments that address regional patient needs. We are driving a range of preclinical and translational research project collaborations with different academic centers across China, Hong Kong, Korea, Singapore, Australia, Japan and Taiwan. In fact, we have a program called StAR [Strategy for Asian Region] with efforts from all of us in Novartis along with these academic investigators to really address Asian cancer patient needs.

Collaboration is critical in helping us understand where the unmet patient needs are, and we have a range of partnerships with stakeholders across the public and private sectors to help us identify gaps and respond appropriately with regionally targeted clinical programs. Over the years, we have also established platforms like the Novartis Asia Pacific Clinical Development Advisory Board (APECHO) to engage medical experts in Asia to uncover opportunities where Novartis and academic institutions/investigators can work together to address unmet medical needs in field of oncology and hematology and how they dovetail with our pipeline and research.

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CAR-T therapy entails drawing blood from the patient via apheresis and separating out the T-cells, which are then cryopreserved, shipped to a facility for genetic reprogramming into CAR-T cells then sent back for infusion into the patient.

Kymriah In Saudi Arabia

Bouchard spotlighted how Novartis' team embarked on the process to register Kymriah in Saudi Arabia in March 2020 - a time around which many countries were heading into, or were already in, lockdown mode.

"Not only did they need to work with the Saudi FDA to establish a framework for the registration of cell and gene therapies, they had to pivot all interactions from face-to-face into virtual," said the executive, who oversees Novartis' oncology business across China, Asia Pacific, Australia, New Zealand, Middle East, Africa and Turkey.

These efforts included collaborations with the Customs and Airport Inspection Authorities for the importation of cells, along with the complexities of onboarding King Faizal Hospital (the Swiss group's Middle East and Africa hub) and its physicians, nurses, pharmacists and coordinators in the administration of the treatment.

"They worked tirelessly and creatively in a challenging situation, making it possible for the first patient to be treated in December of the same year, which is a tremendous achievement," Bouchard declared.

Earlier, Susanne Schaffert, president of oncology at Novartis AG, had similarly outlined how employees had showed unprecedented dedication, with colleagues "getting into their cars and driving to the hospital" to deliver Kymriah; the CAR-T therapy did not miss a single shipment

For example, in our MONALEESA-7 study on breast cancer (an idea generated from APECHO), clinical research uncovered the effectiveness of Kisqali combined with endocrine therapy for pre-menopausal breast cancer populations, where more than 50% of breast cancer incidences in Asia occur in pre-menopausal women.

We have other clinical programs ongoing on common Asian cancer populations like gastric cancer. As we advance our clinical trial and research programs, we also work closely with local governments, national cancer centers and business partners to expand the accessibility of precision oncology, such as biomarker testing which could help identify novel treatments for patients who need them most.

By deepening our understanding of genetic mutations specific to certain regions and ethnicities through our research and clinical programs, we can continue to develop effective therapies in areas such as target, CAR-T/cell and gene, radioligand, and immunotherapy that can truly make a difference to patients in the region.

amid COVID-19, she said in May 2020. (Also see "*Novartis Oncology Head Discusses Cancer Care Challenge With COVID-19*" - Scrip, 21 May, 2020.)

Positive Patient Outcomes

Last year, Novartis received approval for Kymriah in Singapore, representing, at the time, the first commercial CAR-T therapy in Southeast Asia.

On outcomes so far in the island country, Bouchard said that real-world evidence (RWE) data continues to underscore the benefits of Kymriah as seen in the registrational trials, with "equivalent efficacy and improved safety" due to familiarity with cytokine release syndrome and earlier use of the immunosuppressive antibody tocilizumab.

"This has been reflected in feedback from physicians and positive patient outcomes that we have observed in Singapore so far. Across the region we have started a prospective, observational study in patients treated with Kymriah in Asian and Middle-East countries," the executive said. (Also see "*How Novartis Is Tailoring Its Strategy In Asia Pacific, Middle East and Africa*" - Scrip, 22 Dec, 2021.)

The company, he added, constantly analyzes data from pivotal clinical trials, RWE and its manufacturing outcomes to implement adjustments to enhance the manufacturing process and operations.

"Applying learnings from RWE in real-time helps deepen our understanding over time and informs us and physicians on how we can achieve better patient outcomes, " Bouchard emphasized.

Singapore General Hospital (SGH) was the first Kymriah treatment center to become operational in Southeast Asia to treat adult relapsed/refractory DLBCL (diffuse large B-cell lymphoma) and young adult, relapsed/refractory B-cell ALL (acute lymphoblastic leukemia) patients; in October 2021, SGH indicated it had treated around 10 patients with CAR-T cell therapy since the previous year.

More widely, the approval of Kymriah in Australia, Hong Kong SAR, Saudi Arabia, Singapore, South Korea and, most recently, Taiwan, has also paved the way to advance adoption of the CAR-T therapy across the region. The Swiss group has "onboarded" 49 treatment centers to-date, and plans to increase this number within the year.

"For other countries in the region where Kymriah is yet to be approved, we are prioritizing the set-up of regional centers of excellence and treatment centers in Singapore, Hong Kong and Saudi Arabia with the right capabilities and capacity to address the unmet needs of patients from neighboring countries," Bouchard explained.

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Digital Infrastructure

Alongside, digital infrastructure is also being scaled, providing patients and physicians with programs and resources to help them better access CAR-T therapies. A global website, MyTcellTherapies.com, to deliver practical information to patients and healthcare professionals in Asia on ALL , DLBCL and CAR-T therapies, is part of these efforts.

The digital framework is also being tapped to overcome on-ground challenges via the MyTCellTreatment program, a multi-language service that connects home physicians to treating physicians in the centers of excellence. This, the executive explained, eases the "stress and burden" of patients to book travel logistics, while providing patients with “funding guidance” as needed.

Bouchard also sees “great value” in digital therapeutics in the oncology domain for patients and healthcare professionals, and believes they have the potential to enhance care in emerging markets, as well as more developed markets.

He referred to a partnership with Kaiku Health, a Finnish digital health company, for a SaMD (software as a medical device) patient solution to help monitor and manage melanoma, which Novartis is in the process of scaling across the region.

“We also have a broad collaboration in China with Tencent on developing HCP [healthcare professional] and patient portals that can provide more meaningful

Are Health Technology Assessment (HTA) processes somewhat standardized in key AMACO markets or are traditional frameworks still the norm affecting value assessment?

Bouchard: The region has a diverse HTA and pricing and reimbursement landscape. In more established HTA markets like Australia, South Korea and Taiwan, the adoption of precision oncology is more advanced, and in the Middle East we see a wide range of access to precision medicine and movement towards HTA.

However, across the AMACO region, we see that funding for testing continues to limit the use of precision oncology, and there is a lot of scope to improve access to vital technologies such as next-generation sequencing.

In the Middle East and Africa, on one side we have Saudi Arabia and the Gulf countries moving faster than others. Last year, Saudi Arabia announced a move towards setting up an HTA body which will be benchmarked on the top HTA systems worldwide. In the United Arab Emirates, a country with rapid access to medical innovation, precision medicine is already well established, while Egypt, a large country with a population of over 100 million, is undergoing a full transformation of its healthcare system with an ambition to cover its full population by 2032.

As such, all methodologies for access to medicines are being revised. Other countries in the region still have varied access to

information for patient care. We take a market-centric approach to ensuring that solutions effectively meet patients' priority needs."

Reimbursement Systems

Bouchard, who first joined Novartis Canada in 1992 as a market research analyst, also discussed the general reimbursement systems in the AMACO region and payer attitudes towards considering innovative pricing models, including risk-sharing agreements that permit coverage alongside factoring in limited certainty around their financial impact or performance.

Payers in markets such as South Korea, Taiwan and Australia, he indicated, are "increasingly willing to work with us on pioneering ways" to deliver innovative therapies. The Middle East too is seeing rapid movement towards innovative deals in Saudi Arabia, he added, but provided no specifics.

medical innovation with strong regulatory bodies where a significant proportion of access is driven by tenders.

Current HTA approaches and economic evaluation methods may not fully capture the value of precision oncology, often leading to delayed access to these innovative technological treatment platforms. Hence, this requires us to work closely with various government bodies to first set up new frameworks of evaluation.

One-time transformative therapies often require a big shift in thinking about medicines and conventional frameworks of evaluation will need to evolve to reflect this.

"One of the reasons for this shift is because new therapies are offering an unprecedented level of benefit, often to a small number of patients in desperate need, in a small number of highly specialized hospitals. This creates a high demand from patients and society to access these life-changing therapies," he stated.

Novartis is in the process of launching a range of cutting-edge therapies in the region, including Kymriah and the radioligand therapy Lutathera (lutetium Lu 177 dotatate) and also has cancer therapies targeting specific mutations such as Tabrecta (capmatinib) for MET exon 14-skipping non-small cell lung cancer and Piqray (alpelisib) for HR-positive, HER2-negative, PIK3CA-mutated breast cancer.

In the existing portfolio, some recent successes in the region include Kisqali (ribociclib), Revolade (eltrombopag), Tafinlar (dabrafenib)/Mekinist (trametinib) and Jakavi (ruxolitinib); Kisqali, for instance, has a 46% class share across the region in an extremely competitive environment, and an over 50% market share in nine of the markets.

In 2021, nearly 13,000 women in the AMACO region with breast cancer received treatment with

the CDK4/6 inhibitor, “creating a very positive impact on their survival rate," Bouchard added. Kisqali was developed by the Novartis Institutes for BioMedical Research under a collaboration with *Astex Pharmaceuticals*.

Nevertheless, the executive maintained that mainstreaming patient access to these life-saving treatments will require existing reimbursement systems “to be set up to recognize their value. We consistently take an active role in partnering with reimbursement bodies, to overcome barriers and facilitate access to deliver our life-saving treatments to patients and HCPs,” he declared.

Fundamentally, this involves a partnership-based approach to improve access for patients, whether through tiered pricing models, sharing the cost of medicines with government healthcare systems, charities and other payers, or directly with patients without healthcare coverage who are unable to pay for the full cost of their medication.

Partnering Efforts

Meanwhile, in addition to market opportunities, the Swiss group also appears to be open to building on partnerships to bolster its pipeline across the AMACO region where cancer incidences account for over half of global cases and unmet patient needs are high.

“Within Asia, the Middle East and Africa regions, we are specifically interested in collaborations in gastric cancer and hepatocellular carcinoma, which have an over-proportional incidence in this geography,” Bouchard said, but also underscored "the breadth and depth" of Novartis’ own portfolio of assets.

Last year, the company signed an option and license agreement with *BeiGene, Ltd.* for the Chinese firm’s TIGIT inhibitor ociperlimab; the partners already are working together on the development of the PD-1 inhibitor tislelizumab that is now under review in the US for esophageal cancer. (Also see "*Novartis Expands BeiGene Tie-Up To TIGIT Inhibitor In $1bn-Plus Option Deal*" - Scrip, 21 Dec, 2021.)

Novartis’s John Tsai On The Four Philosophies Driving R&D

By Mandy Jackson

31 Jan 2022
Scrip spoke with global development head and chief medical officer John Tsai about the factors Novartis considers when it decides which R&D programs to advance, including externally sourced assets.

Read the full article here

Novartis global development head and chief medical officer, John Tsai, had earlier maintained that in oncology, and across its four other therapeutic areas (cardiology/metabolism/renal, immunology, neurology and hematology), the company remains agnostic about where its science

comes from, whether it originates from the company's own research labs or from external sources.

"What we want to do is to drive the best innovation for advancing these five therapeutic areas," Tsai said at the time.