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Life & Health Underwriting Insights

Messenger RNA – the new kid on the block?

When pharmaceutical companies gathered at a White House roundtable in March to discuss efforts to develop a vaccine, companies using messenger RNA-based (mRNA) platforms were clearly ahead of the pack. Their clinical studies had already started, and they promised to deliver a vaccine fast. This front-leading position was confirmed in April, when the Federal Biomedical Advanced Research and Development Authority (BARDA) awarded the leading mRNA firm, Moderna, USD 483 million – roughly half of what the federal agency was spending – to accelerate the development of a COVID-19 vaccine[1].

COVID-19 has brought mRNA therapies front and center in public policy. Not only does mRNA technology have the potential to produce the first COVID-19 vaccine, but it could become the preferred fast track vaccine production method against novel viruses in the future.

We want to leverage this momentum and bring mRNA therapies onto insurers' radars.

Why? Beyond vaccines for emerging infectious diseases, mRNA technology may play a key role in developing vaccines for cancer – substantially contributing to the success of immunotherapy for cancer patients. Furthermore, mRNA therapy could become vital for a variety of inherited or acquired diseases where targeted expressions of proteins are needed.

The front runner: mRNA therapies that encode proteins

The conventional view of the central dogma of molecular genetic puts RNA in a supporting role – the intermediary between DNA and proteins, a passive messenger for information. But in addition to carrying instructions for making proteins, RNA can turn genes on and off and slice and dice other RNA strands. There are several categories of RNA therapies, including hybrid approaches that combine several therapies into a single package.[2] This article focuses on the mRNA therapy which is proving to be most impactful: mRNA that encodes proteins. This technique is being used to develop vaccines for viral diseases, for personalised cancer treatments and as substitute for protein-replacement therapies for rare diseases. This category of mRNA therapy is proving to be the most impactful.

Expanding the pipeline

mRNA therapies dominate headlines about the race for a COVID-19 vaccine, but no antiviral mRNA vaccine has yet reached market approval. However, preliminary pre-clinical testing of mRNA vaccines in animals and humans has been successful. A few prominent examples include animal experiments for SARS and MERS and, pre-clinical human studies with Zika, Chikungunya and Dengue. Additional pre-clinical studies are under way for Rabies, CMV and influenza.[3,4]

While mRNA vaccines have demonstrated success against infectious diseases, using vaccines to cure cancer has been less promising. For 20 years, scientists have dreamed of creating vaccines that teach the body to destroy tumors. After hundreds of clinical trials, not a single vaccine has been approved to treat cancer. Only the recent success and Nobel prize for immune checkpoint inhibitors have established immunotherapy as preferred therapy to treat or cure certain responsive cancers. These new developments are opening possibilities for treating cancer with mRNA vaccines.

Improving outcomes with cancer vaccines

Immune checkpoint inhibitors have revolutionised the treatment of several leading cancers. Immune checkpoint inhibitors are now approved to treat some patients with melanoma, breast cancer, bladder cancer and cervical cancer. Blocking antibodies to CTLA-4 and PD-1/PD-L1 have improved survival for many patients and long-term durable responses have been achieved in "responder" patients – patients who respond to a treatment. However, only a minority of cancer patients are responders. We see a role for cancer vaccines to boost the response and increase the fraction of cured patients, thereby improving health outcomes for more people. Personalised immunotherapy, tailor-made to match the genetic profile of a person's cancer, elevates immunity against the mutated portions of their tumor. A patient's risk of developing new metastatic lesions will be significantly reduced and therefore increases the chances of successful treatment.[5] But personalised immunotherapy treatment is expensive. Private public partnerships solutions might be needed to help finance personalised treatment for more patients.

Beyond vaccines: mRNA to treat rare inherited diseases

Outside of infectious diseases or cancer vaccines, mRNA technologies will become a powerful option to treat rare inherited diseases, like orphan disease. Messenger RNA therapy can be used to produce a missing or defective protein, which causes a disease phenotype. Selective protein expression in ageing tissue such as muscle, cartilage or retina by mRNA injection might become useful in regenerative medicine.

mRNA therapy has demonstrated potential for three rare metabolic disorders: methylmalonic acidemia, acute intermittent porphyria and Fabry disease, but it has failed so far for Crigler-Najjar syndrome.[3] In the three success stories, mRNA therapy restores functional protein in target organs. Although traditional gene therapy using CRISPR-CAS methodology could correct a mutation permanently, rather than temporarily as in mRNA therapy, the risk of collateral mutations inserted by gene therapy is feared. Regulators still ban 'editing' of human DNA to avoid unethical tampering with hereditary traits and payment schemes with healthcare providers for gene therapy are uncertain. mRNA therapy is more practical, and we expect its use for treating metabolic disorders to grow over the coming years, especially in the absence of widespread acceptance and use of gene therapy, particularly as gene therapy's potential remains stunted.

The new kid on the block has long-term potential

If mRNA COVID-19 vaccines turn out to be successful and if they are delivered fast, in the desired number of doses and at an affordable price, then we may begin to see mRNA leveraged more frequently in healthcare – and not just for fighting infectious diseases. If mRNA proves useful in combatting the current pandemic, it will also gain traction in in the fields of cancer of inherited diseases.

Large scale use of mRNA cancer vaccines may require the industry to change the way we underwrite cancer survivors. Traditionally, after surgery, chemotherapy and radiation, survival and relapse rates were defined by type, histology and stage of a malignant tumor. In the new era of cancer immunotherapy, a patient with an advanced stage of malignant melanoma with significant metastasis – but who has responded to immunotherapies – may become a long-term survivor and be considered an insurable risk. In the coming decades, mRNA cancer vaccines may increase the percentage of immunotherapy responders. To continue to expand insurability and make the world more resilient, it is essential for the industry to become an early adopter of these medical advancements as they unfold. We continue to monitor developments in mRNA cancer vaccines and adapt our guidance in Life Guide to reflect the latest medical developments.

Questions or feedback: Contact RnD_underwriting@swissre.com

References

1 Cohen, J. Vaccine designers take first shots at COVID-19. Science 368, 14-16 (2020).
2 Adams, D., et al. Patisiran, an RNAi Therapeutic, for Hereditary Transthyretin Amyloidosis. N Engl J Med 379, 11-21 (2018).
3 Garde, D. Key partner cuts ties with brash biotech startup Moderna, raising big questions about its pipeline. STAT (2017).
4 Richner, J.M., et al. Modified mRNA Vaccines Protect against Zika Virus Infection. Cell 168, 1114-1125 e1110 (2017).
5 Pardi, N., Hogan, M.J., Porter, F.W. & Weissman, D. mRNA vaccines - a new era in vaccinology. Nat Rev Drug Discov 17, 261-279 (2018).

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