

James R. Berenson, MD, CEO & President Institute for Myeloma & Bone Cancer Research (IMBCR)



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Founded in 2003 by James R. Berenson, the IMBCR is an independent, non-profit cancer research institute that is dedicated to ultimately finding a cure for multiple myeloma. The IMBCR conducts preclinical research that is related to multiple myeloma and metastatic bone cancer both in vitro and in vivo. Having spent more than 28 years working closely on myeloma and bone cancer, Dr. Berenson has been able to influence the advancement

of treatment for these debilitating diseases. Several breakthroughs the IMBCR has accomplished over the last year include identifying a new target that, when blocked, treats myeloma directly and stops the formation of early blood vessels that feed myeloma; developing a peptide that blocks myeloma growth directly; and is leading the ongoing initiative, “The Cure Myeloma Project”. In addition to his responsibilities at the IMBCR, Dr. Berenson is also President and Chief Executive Officer of Oncotherapeutics, Inc., a corporation that conducts clinical trials throughout the United States that are related to myeloma and metastatic bone disease as well as other cancers.

OBR: *Tell us about your mouse models and how you use them to study myeloma.*

JRB: We take samples of bone marrow from myeloma patients and then grow them in immunodeficient mice. We have about ten different tumors growing over a long period of time and we test different drugs and drug combinations. Outside of the traditional academic setting with their many committees and large infrastructure, we can get things done in weeks that usually take 6-12 months in an academic setting. Thus, in a much quicker time, we are able to provide answers to pharmaceutical and biotech companies about whether their drugs have potential anti-tumor activity as well as at least early signs of safety either with their drug alone or in combination. Our models are faithful, in that if a patient is resistant to drug A, then when we test drug A in the animal model containing that same tumor, the results are very consistent to the effects of that drug in the patient. We are able to develop novel combinations and say to the company: “Why don’t you use these drugs or why don’t we test this regimen in the clinic?”

OBR: *Have you used your data to conduct clinical trials?*

JRB: Yes. We have a contract research organization (CRO) group called Oncotherapeutics. It is

a for-profit company that does clinical research with about 125 groups around the country. We conduct many different types of trials in cancer patients with a variety of types of agents either alone or in combination therapies. I tend to act as principal investigator on the trials in myeloma or metastatic bone since that is my area of expertise. If there are any other cancers, I’ll bring in an expert on that specific disease.

OBR: *Can you give me an example of moving from mouse into clinical trial?*

JRB: Novartis has a new drug which is being developed and has a quite similar mechanism to a drug from Merck recently approved by the FDA. These drugs are called histone deacetylase inhibitors. We showed first in the test tube and then in our animal models that by combining this new drug with the old chemotherapeutic agent melphalan that this was very synergistic and well-tolerated. We are submitting this laboratory work for publication, but at the same time have been given the green light to conduct a Phase 1 clinical trial to develop this combination for the treatment of myeloma patients. This is most exciting.

I can give you many other similar examples. The Velcade/melphalan combination for myeloma—which has been recently studied in a large,



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international, randomized Phase 3 trial—that original concept came out of preclinical work we did in the laboratory several years ago. We conducted our own clinical trials, and the combination worked quite well in the relapsed/refractory setting where we established the maximal tolerated dose in the Phase 1 trial. Next, we performed a front-line Phase 2 study. We presented the data at the Annual Meeting of the American Society of Hematology (ASH) in December. We’re just about to publish the results of that front-line study with very positive results—very active and well-tolerated.

OBR: *Is your success in this area leading to other developments?*

JRB: What has been very gratifying is that through this research we’ve been able to identify new targets. For example, we’ve recently published data to show that if we stop production of the protein pleiotrophin or PTN—which we’ve identified as over-expressed in myeloma patients—we can stop myeloma growth. In addition, we have shown that PTN can transform a white cell into a blood vessel cell. We presented this work at the ASH. PTN is not only a target for treating myeloma, but we have shown again with our animal models that the same principle holds true when we’ve evaluated breast cancer and tried to get PTN to grow blood vessels—the same protein is made by breast cancer.

OBR: *How did you discover this protein?*

JRB: We didn’t discover it. We’re collaborating with Dr. Tom Deuel at Scripps Clinic and he originally isolated the protein. But the news, if you will, is that we’ve now uncovered the fact that tumors make a lot of PTN and when they produce it, this can turn a specific type of white cell called a monocyte into blood vessel cells. So there has been some thought that the earliest cells in the formation of the blood vessel are in the blood, not in your blood vessel, and that’s a monocyte. Thus, we have shown that PTN can cause transdifferentiation, that is, in a Houdini-like manner turn a white cell into a blood vessel.

OBR: *And we imagine the success with myeloma will lead to other predictive mouse models in other tumor types.*

JRB: The tumors we have grown to date have been from our myeloma population in the clinic. We are beginning to look at other tumors, but these are not our own patients’ tumors and many of these are developed from other established cell lines. We are going to start beginning the same process and hope for similar success.

OBR: *Earlier, you indicated personalized medicine in oncology is exciting. Would you categorize what you do as personalized?*

JRB: I would categorize this research as moving toward personalized medicine but not personalized yet. Hopefully, we are going to have categories of patients that show a similar pattern in terms of expression of proteins or genes indicating resistance to drugs and the knowledge of what drugs to use to overcome that resistance. In one patient it may be one drug and in a different genetic profile it may be another or a combination of agents. But I certainly am very excited that this research is helping me expand the different cocktails that we can evaluate in our patients very quickly. For me, as I like to say, it’s not about complete remission, it’s about patients having a complete life.

OBR: *You see a lot of room for improvement in targeting?*

JRB: Everyday when I go to clinic and see the neuropathy caused by some of the drugs or the poor blood counts for myeloma or the gastrointestinal (GI) side effects, I just shake my head and say we can do better. I am interested in developing and finding new targets and in optimizing combinations of drugs to bring the levels of drugs in patients down. It may be that you can bring both drug levels down and the drugs may work better together. For example, our work combining Velcade with either Doxil or melphalan are good examples of this concept.

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OBR: *How do you fund your research?*

JRB: The IMBCR is a non-profit organization and is funded with donations from grateful patients, family members and large foundations including the Annenberg, Skirball and Kramer Foundations. We are open to any philanthropic organization that can contribute to our work. We also apply for grants and we do contract work with the pharmaceutical companies. In terms of the clinical trials, we contract and perform the work required but I also like to work in the practice setting. I see patients every day in the clinic many of whom are on clinical trials. This allows me to get a direct “feel” for the effectiveness of these treatments both in terms of efficacy and safety. The motivation for the work in my clinic is certainly not economic, but I am really interested in giving top clinical care while conducting clinical research ultimately making sure that people are taken care of in a positive manner while helping aid the development of new treatments.

OBR: *What do you want to see the Institute accomplish in the near future?*

JRB: I want the Institute to grow, to be able to develop already-existing therapies with better and more ways to perform preclinical work with many more agents. I also want to be able to identify new targets. For example, we have a very exciting project, we call the Cure Myeloma Project, where we are developing a therapy that will specifically only knock out the myeloma cells and leave the rest of the body alone. This will then be truly targeted therapy leading to effective therapy without impacting negatively the patient’s quality of life. Indeed, ultimately that is the goal of our therapies for cancer patients. **OBR**

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