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A roadmap for cost-of-goods planning to guide economic production of cell therapy products

YONATAN Y. LIPSITZ[1], WILLIAM D. MILLIGAN[2], IAN FITZPATRICK[3], EVELIEN STALMEIJER[4], SUZANNE S. FARID[5], KAH YONG TAN[6], DAVID SMITH[7], ROBERT PERRY[8], JESSICA CARMEN[9], ALLEN CHEN[6], CHARLES MOONEY[10] & JOHN FINK[11]

*[1]Institute for Biomaterials and Biomedical Engineering, University of Toronto, Toronto, Canada, [2]Steminent Biotherapeutics, Taipei, Taiwan, [3]Scinogy Pty Ltd, Melbourne, Australia, [4]eXmoor Pharma Concepts, Berkshire, United Kingdom, [5]University College London, London, United Kingdom, [6]Bioprocessing Technology Institute, A*STAR, Singapore, [7]PCT, a Caladrius Company, Allendale, New Jersey, USA, [8]Atara Biotherapeutics, San Francisco, California, USA, [9]MaxCyte, Gaithersburg, Maryland, USA, [10]Oklahoma Blood Institute, Oklahoma City, USA, and [11]Brooks Automation, Chelmsford, Massachusetts, USA*

Abstract

Cell therapy products are frequently developed and produced without incorporating cost considerations into process development, contributing to prohibitively costly products. Herein we contextualize individual process development decisions within a broad framework for cost-efficient therapeutic manufacturing. This roadmap guides the analysis of cost of goods (COG) arising from tissue procurement, material acquisition, facility operation, production, and storage. We present the specific COG considerations related to each of these elements as identified through a 2013 International Society for Cellular Therapy COG survey, highlighting the differences between autologous and allogeneic products. Planning and accounting for COG at each step in the production process could reduce costs, allowing for more affordable market pricing to improve the long-term viability of the cell therapy product and facilitate broader patient access to novel and transformative cell therapies.

Key Words: *cell therapy, cost of goods, COG, autologous cell products, allogeneic cell products, tissue procurement, material costs, facility costs, production costs, storage*

Introduction

Current and expected pricing for approved and late-stage cellular therapy products reflect the high cost of goods (COG) used today to produce most therapies (Figure 1). Optimizing COG will promote the development and commercialization of more affordable cell therapy products, which in turn are more likely to achieve reimbursement from payers and gain broader adoption for patient treatment [6]. Ideally, the economic aspects of a product will be addressed from the very beginning of development to enable a viable, profitable product life cycle because process changes become more difficult as development progresses. A robust cell therapy business model cannot be fully realized without addressing every cost-relevant "needle-to-needle" consideration. Starting from cell sourcing through to manufacturing, distribution, and finally clinical application, COG optimization aims to minimize the cost per unit of cells and ultimately the cost per dose while maintaining product quality.

In June 2013, a survey was distributed to the International Society for Cellular Therapy (ISCT) membership asking about the COG breakdown in therapies under development by member organizations (see supplemental Figure S1 for survey overview). The survey results indicated that commonalities can be drawn between process components of similar cell products. The two main cell therapy modalities, allogeneic (donor to patient) and autologous (patient to self), necessitate different "needle-to-needle" pathways (Figure 2). The production process differences between manufacturing strategies used for allogeneic products and the patient-specific manufacturing strategies used for autologous products result in distinct COG optimization decisions. Notably, allogeneic

Correspondence: **Yonatan Y. Lipsitz**, PhD, Institute for Biomaterials and Biomedical Engineering, University of Toronto, 164 College Street, Toronto, Ontario, Canada M5S 3G9. E-mail: yonatan.lipsitz@mail.utoronto.ca

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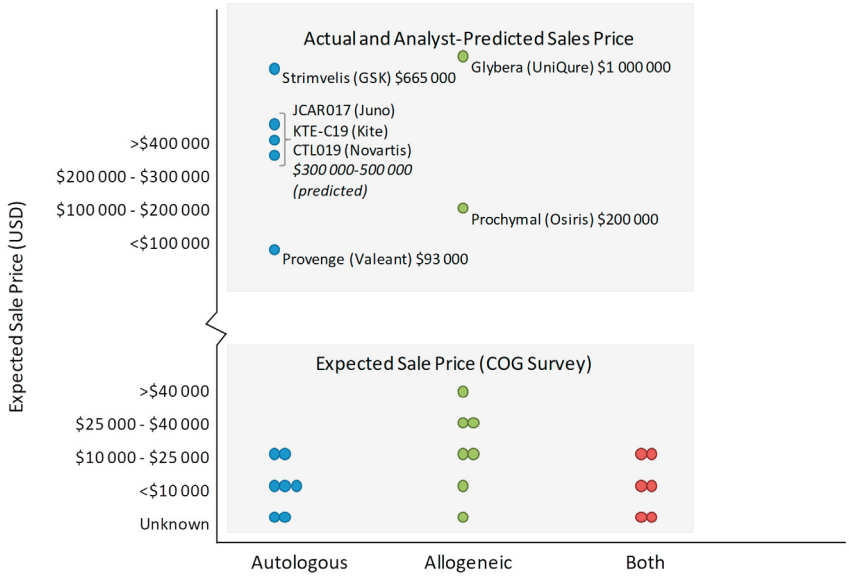

Figure 1. Sales price of autologous and allogeneic cell therapies. Expected sales prices from the COG survey in 2013 are compared with published and anticipated costs for therapies approved or in trials. Prices for Glybera, Strimvelis, Prochymal and Provenge are based on published prices from each company. Analyst reports of expected chimeric antigen receptor T-Cell prices range from $300 000 to 500 000 [1–4]. While these prices have not been confirmed by the companies developing these therapies, the $800 000 cost of stem cell transplants has been seen as a benchmark for these therapies [5].

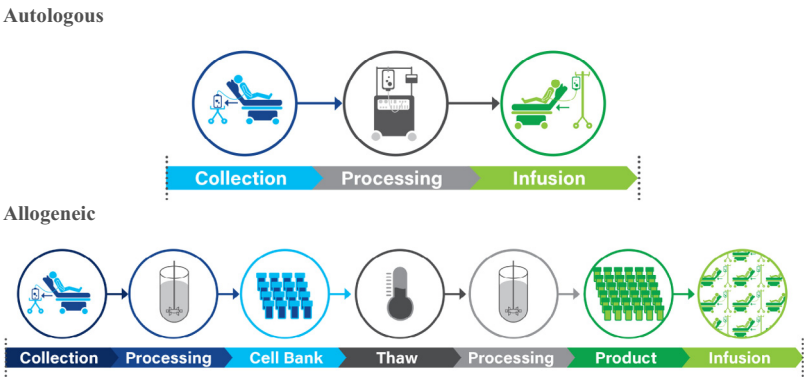

Figure 2. Allogeneic versus autologous manufacturing models. In allogeneic therapies, a single sample is saved in a master cell bank from which a working cell bank is used for manufacturing. These therapies are then distributed to large patient populations. In autologous therapies, each single patient sample is manufactured into a product that is used to treat a single patient.

products benefit highly from economies of scale in a similar manner to traditional pharmaceuticals, whereas costs are relatively consistent as autologous products are scaled out.

In this article, we outline a COG roadmap of key considerations and objectives for each step in cell manufacturing to plan for reduced COG, enable lower product pricing, and improve patient access. Designed to inform early process development of the connection between each development decision and the eventual cost-efficiency of the final therapy, this roadmap augments the ISCT COG survey results with relevant published references on how to address the challenges encountered with each manufacturing step (Figure 3).

COG impact analysis for cell therapy products

When beginning translation of a preclinical process to clinical production, the various manufacturing methods available can significantly influence the final COG at commercial scale. Impact analysis is a valuable tool to understand the sensitivity of the final COG in response to different manufacturing strategies and product demand scenarios forecast at the end of the expected decade of development of a cell therapy