Challenges and Opportunities with Patient-Centric Drug Product Design: Industry Perspectives

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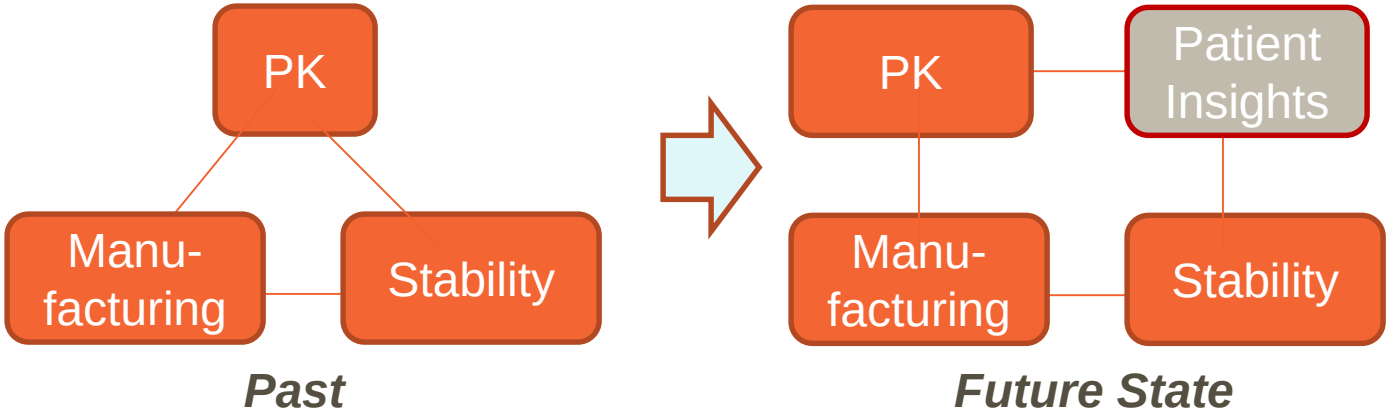
Matthew Burke, Ph.D.

The simplified drug product ambition



CDER Patient-Focused Drug Development

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Patient-focused drug development (PFDD) is a systematic approach to help ensure that patients' experiences, perspectives, needs, and priorities are captured and meaningfully incorporated into drug development and evaluation. As experts in what it is like to live with their condition, patients are uniquely positioned to inform the understanding of the therapeutic context for drug development and evaluation.

https://www.fda.gov/Drugs/DevelopmentApprovalProcess/ucm579400.htm

Language – what does patient focused/patient centric actually mean?

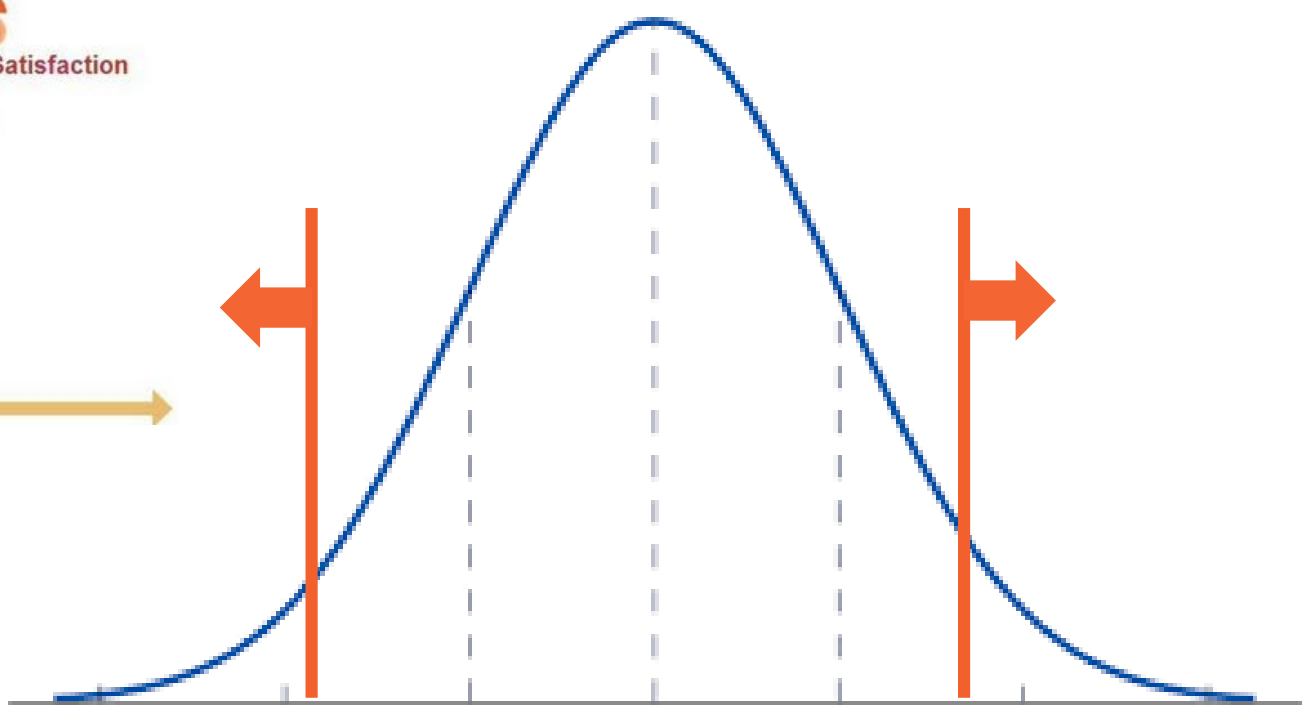
- The National Health Council defines patient centered as: Any process, program, or decision focused on patients in which patients play an active role as ***meaningfully engaged participants*** and the central focus is on optimizing the use of patient-provided information.
  http://www.nationalhealthcouncil.org/sites/default/files/Value-Rubric.pdf

- A ***patient centric drug product design*** definition proposed by Drumond et al. "The process of identifying the comprehensive needs of individuals or the target patient population and utilizing the identified needs to design pharmaceutical drug products that provide the best overall benefit over the intended duration of treatment"

  Drumond et al Int J Pharm, 521:294-305 (2017)

- The core intent of these definitions focuses on doing things ***with*** **patients** – not *for* or *to* patients -- and it relies on **meaningful, direct patient** engagement.

The change curve & most frequent thoughts



Age Range

- Age & Inclusivity: Pediatric or elderly population
- Devices: Human factors

Examples to learn from: Was it serendipity or design?

- A past review by Drumond et al captures information on patient acceptability of pharmaceutical products
- For most commercial products, it is difficult to conclude if a patient-centric drug product presentation was a result of serendipity or intentional design

Copaxone Injectable

	COPAXONE® 20 mg	COPAXONE® 40 mg
Approval	1996	2014
Administration	**Daily** injection	**3-times-a-week** injection at least 48 hours apart
Dose	**20 mg** of glatiramer acetate	**40 mg** of glatiramer acetate
	1 ml — 20 mg — 40 mg	**Both COPAXONE® 20 mg and COPAXONE® 40 mg formulations have the same volume of liquid in the syringe.**
Packaging	• **30** pre-filled syringes in a 1-month supply	• **12** pre-filled syringes in a 1-month supply
Injection Type	For subcutaneous (fatty layer under the skin) injection only	
Delivery	Both doses can be used with **auto***ject*® 2 *for glass syringe* Not actual size. Free with a prescription from your physician. Call **Shared Solutions®** at **1-800-887-8100**.	

Inhaled Insulin

Dance 501:
A Patient-Friendly Approach

A needle-free, pain-free, tasteless insulin delivery system

Octreotide Implant

Importance of the Target Product Profile (TPP)

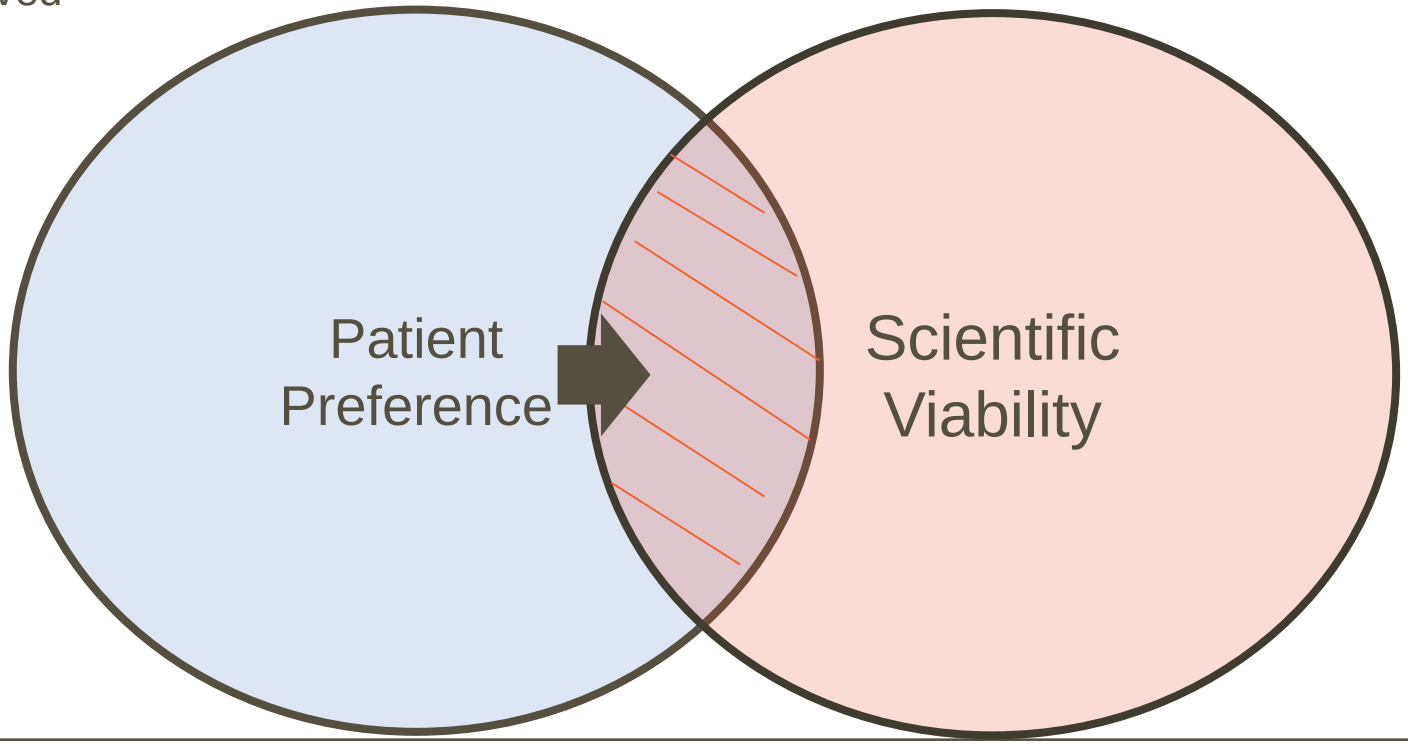
- The tangible implementation of patient centric drug product design typically occurs in the pharmaceutical development departments

- Input from a multi-disciplinary community:
  - External stakeholders such as patients, care givers, regulators, and health care professionals
  - Internal departments such as commercial, marketing, clinical, regulatory, manufacturing, packaging, etc.
  - Other scientific disciplines, such as ethnography, epidemiology, psychology, industrial design, digital experts, etc..

- This network of information is translated into the Target Product Profile at the start of development of a new medicine and is refined as new data is generated during the development cycle.

What are the implementation challenges?

- Creation of the physical drug product is a detailed, technical process often not fully visible or understood by the wider multi-disciplinary community
- It is vitally important that the patient research and insights do not become lost in the technical compromises that are inevitable during the development of a new medicine.
- Simple first steps like the methodologies and techniques to collect the data need to be improved



Methodologies – the weakest link?

Appendix 2: Subject Taste Questionnaire

Subject No: _____ Date: _____

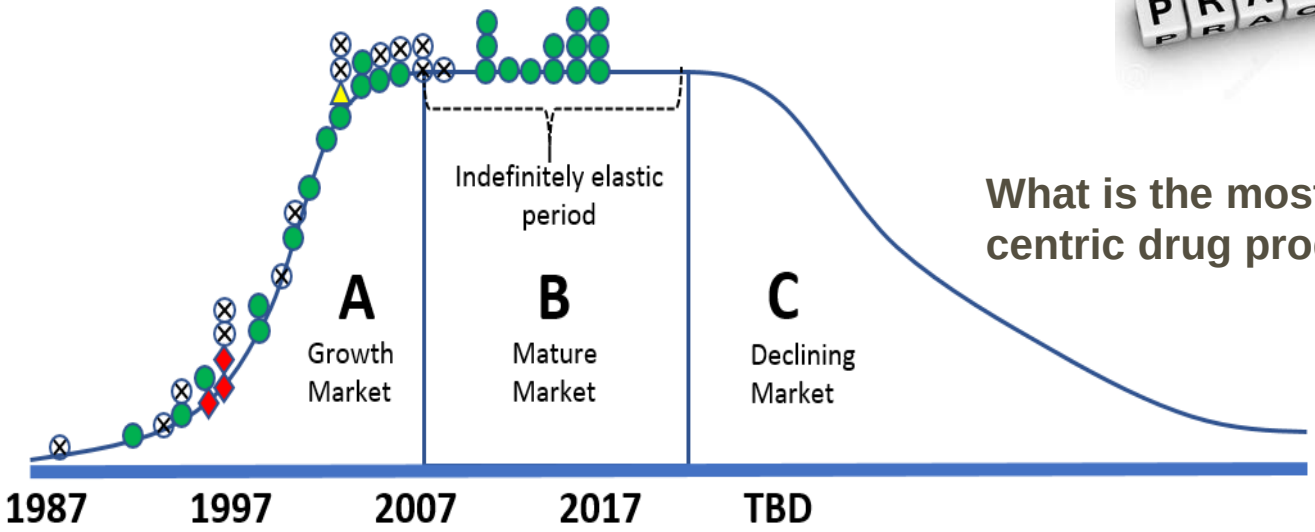
1. **Describe the taste you are experiencing:**
   - Bitter_____
   - Salty_____
   - Sour_____
   - Sweet_____
   - Other _____

My Mistake!

2. **How do you assess the taste in your mouth at this moment?**

Scale	Definition	Feeling	30 seconds	2 minutes	5 minutes
1	a very good taste	!! !!			
2	fair-pleasant, "not bad for medicine"				
3	acceptable, some bad taste				
4	very poor, some aversion to taking the product				
5	horrible, a very bad taste				

HIV Case Study

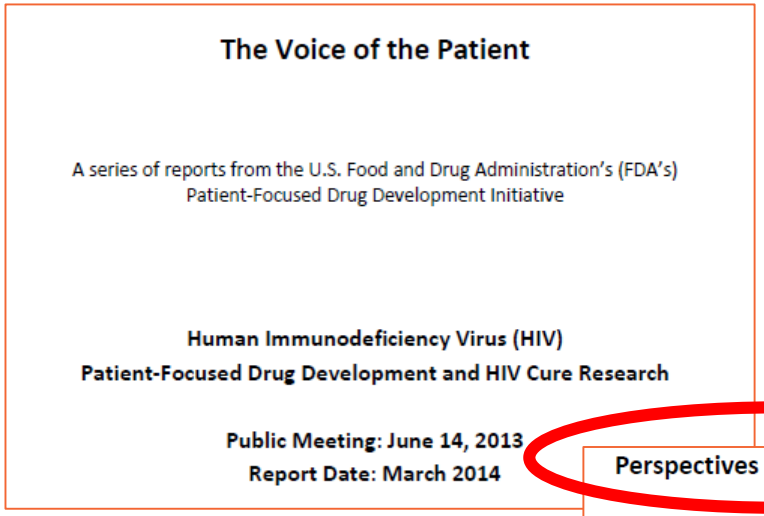


What is the most patient centric drug product for HIV patients?

HIV product approvals between 1987 and 2017.

(●) represents a once daily oral product approval
(◆) represents a three times a day oral product approval
(⊗) represents a twice a day product approval
(▲) represents a twice a day injection approval

Where should we begin?



The Voice of the Patient

A series of reports from the U.S. Food and Drug Administration's (FDA's) Patient-Focused Drug Development Initiative

Human Immunodeficiency Virus (HIV)
Patient-Focused Drug Development and HIV Cure Research

Public Meeting: June 14, 2013
Report Date: March 2014

Perspectives on ideal treatment

When asked for their thoughts on how current therapies could improve (i.e., what are patients looking for in an "ideal treatment"), participants commented on the following:

- **Formulations** of potential new products that could help minimize non-adherence were frequently mentioned. Many patients pointed out that an ideal treatment would be a long-acting product that would limit the number of times patients must take a dose. One patient noted that other conditions, such as osteoporosis, have treatments that are only dosed weekly or monthly and asked, "Why can't we get to that for HIV?" Another patient noted that developing treatments for, say, cardiovascular conditions alongside of HIV in a single dosage would "start to address the adherence question."

Long Acting Products

https://www.fda.gov/ForIndustry/UserFees/PrescriptionDrugUserFee/ucm368342.htm

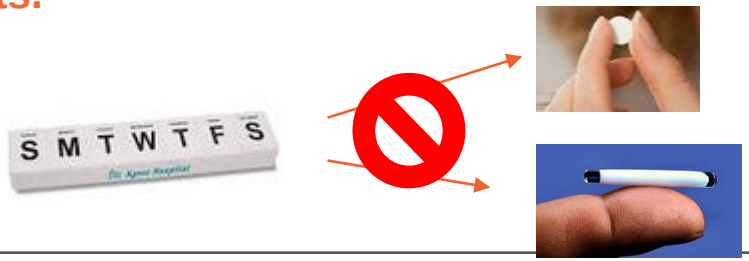
Which long acting drug product is preferred?

Conference on Retroviruses and Opportunistic Infections (***CROI***) 2017

- a poster by Ostermann et al. entitled “Who wants to switch? Gauging interest in potential new antiretroviral therapies”
  - In-person surveys were conducted with 263 HIV infected patients

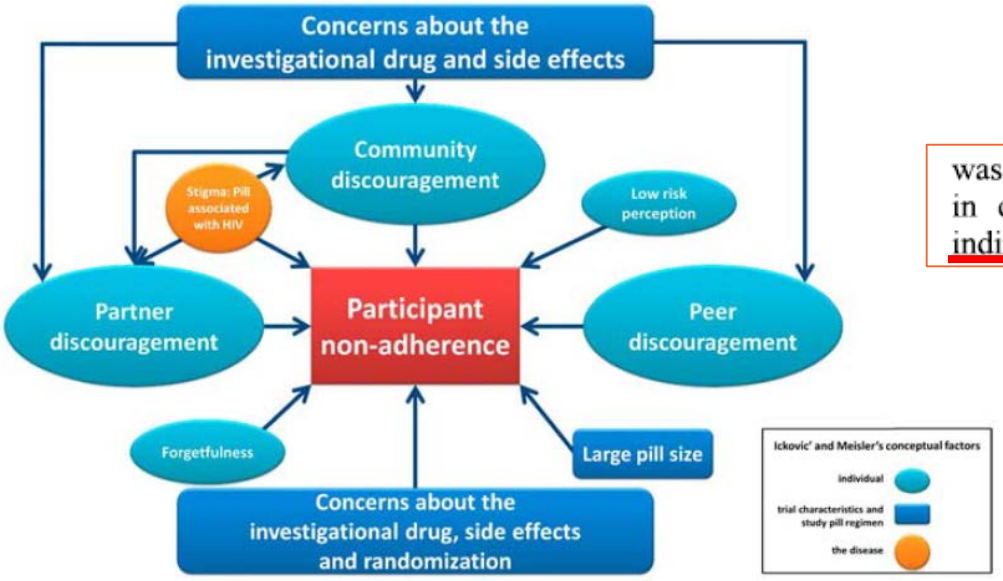
- Patients prescribed a one-pill-once-a-day regimen were likely to exhibit *an interest* in switching to a **one-pill-once-a week** or **to implants dosed every six months**.

- On the other hand, subsets of HIV patients with an **AIDS diagnosis** **were less interested in switching to weekly pills** and **exhibited no interest in switching to implants.**



Can one type of drug product be appropriate for all patients?

Country/Region considerations



Kenya and South Africa

was told not to take the pill). Women's narratives in the SSIs, in contrast, provided rich illustrations of the direct and indirect influence of others on participants' nonadherence.

EPIDEMIOLOGY AND PREVENTION

Participants' Explanations for Nonadherence in the FEM-PrEP Clinical Trial

Amy Corneli, PhD, MPH,† Brian Perry, MPH,* Kevin McKenna, MPH,*‡ Kawango Agot, PhD, MPH,§ Khatija Ahmed, MBChB, MMed Micro,‖ Jamilah Taylor, BA,* Fulufhelo Malamatsho, BSocSci,‖ Jacob Odhiambo, MA,§ Joseph Skhosana, BTechBioSci,‖ and Lut Van Damme, MD, MS, PhD¶#*

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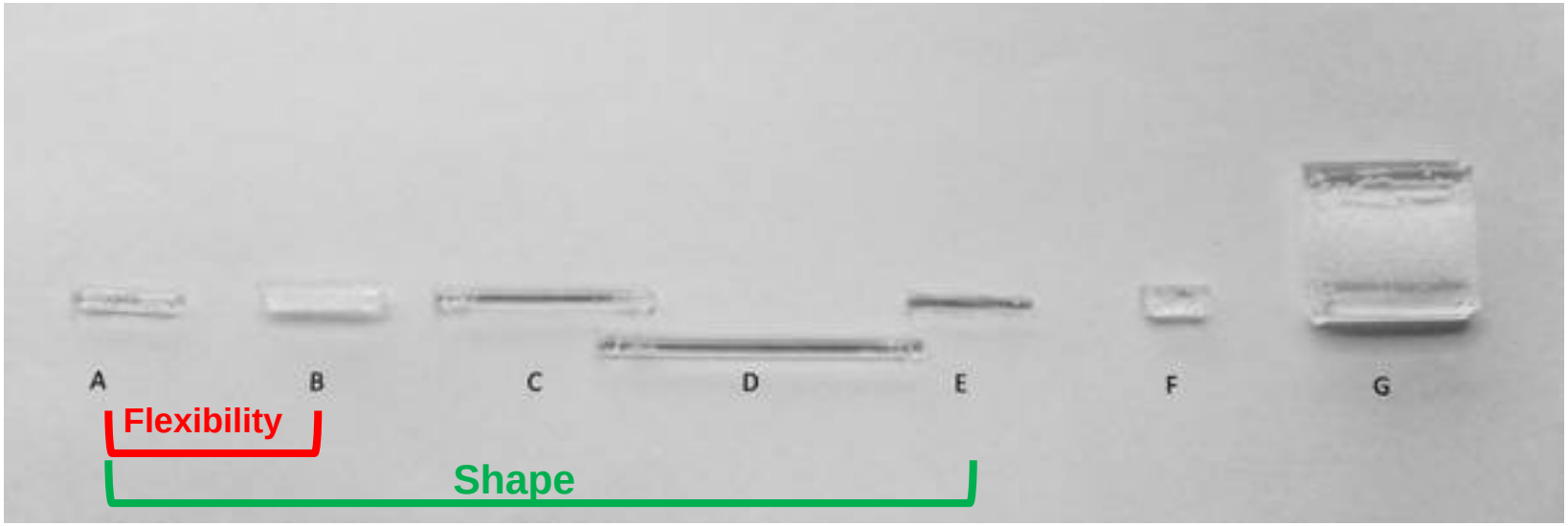
More detailed patient insights - implants



A
Silicone
2cm length
2.5mm width
2.0mm height
Cuboid

B
PLGA
2cm length
2.5mm width
2.0mm height
Cuboid

C
Silicone
4cm length
2.5mm width
2.0mm height
Cuboid

D
Silicone
6cm length
2.5mm width
2.0mm height
Cuboid

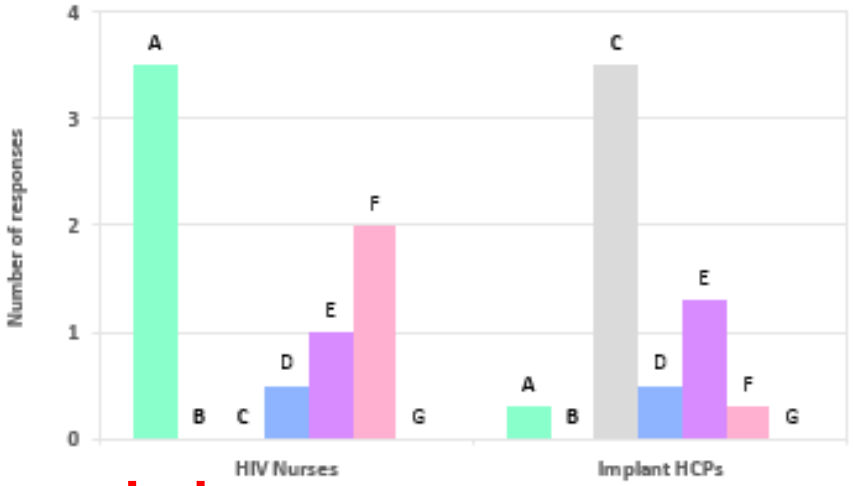
E
Silicone
2cm length
2.5mm diameter
Rod

F
Silicone
2cm length
5.5mm width
2.3mm height
Microchip

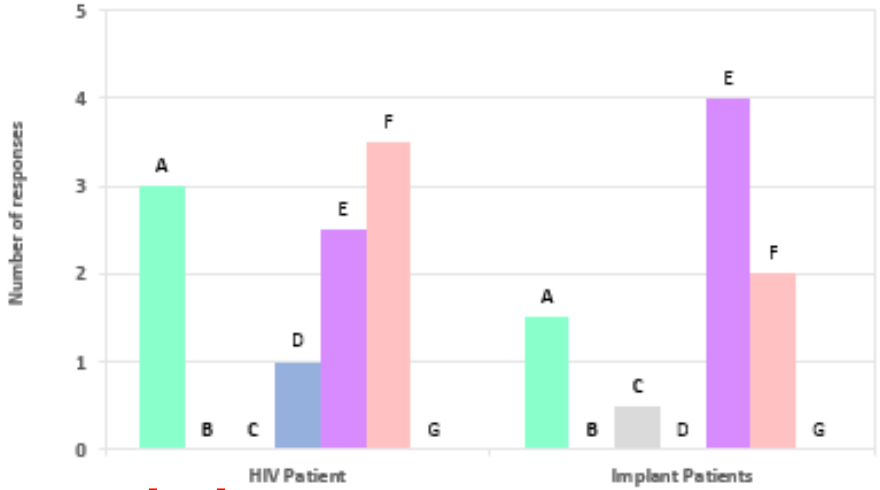
G
Silicone
5cm length
5cm width
1.5 cm height
Macrochip

More detailed patient insights - implants

HCP preference



Patient preference



Experience levels

More detailed patient insights - implants

- Patient interest to palpate the implant daily to provide assurance to the patient that the drug was still “working”

- Noted that a reduction in implant size over time for a biodegradable implant, could lead to the perception of no longer receiving the treatment

- Patient preference between implants requiring surgical removal/retrieval versus one that did not require retrieval, **the choice was clearly for a biodegradable implant that did not require retrieval**

Disruptive Technical or Clinical Factors

- For example, what if our HIV molecule demonstrates unexpected benefits for oncology patients to reduce tumor size in an early clinical trial
- Is an implant appropriate for oncology?

- What is the NEW drug product development strategy?
- Not an uncommon challenge and requires nimble development to enable patient-centered designs without the need for restarting the entire development and clinical process

Opportunities

- Most stakeholders believe that the information collected from patients should be made accessible across the industry for the benefit of all patients.
  - The FDA, in the June 2018 draft guidance *Patient-Focused Drug Development: Collecting Comprehensive and Representative Input*, "**encourages collaboration** among multiple stakeholders and the use of methods to combine and reuse existing data (e.g., national registry data, archival databases) to fit the specific needs of the research question(s) and study goals."
  - Websites such as *https://clinicalstudydatarequest.com* already collect clinical information allowing researchers an avenue for data mining from anonymized sources, offering a potential prototype for the collection and sharing of patient insights from the clinic, human factors or real world use

Recommendation:

- The creation of a centralized public database could greatly increase the visibility and diversity of patient insights while reducing the burden to patient organizations
- Standardized and unbiased data collection methods could be developed and made available as part of the database to encourage consistent study designs
- Encourage independent patient advocacy groups to conduct studies to build upon the existing data set in a consistent manner

Concluding Thoughts

- Working *with* patients during product development will be critical to design successful medicines
- Recommend a cross industry patient insights database
- Consider more than one drug product design when appropriate

Acknowledgments & Questions

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Please contact: matthew.d.burke@gsk.com if you are interested in joining the IQ patient centric working group