ASCPT

FROM MOLECULE TO PATIENT

ASCPT 2019 ANNUAL MEETING

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Will antibody-based anti-infective therapies save conventional treatment failures?

---Opportunities and challenges of development of antibody-based anti-infective therapies

2019 ASCPT Annual Meeting

March 16th 2019

Why do We Need New Anti-infective Therapies?

- Emerging drug resistance
  - Carbapenem resistance
  - HIV drug resistance has increased from 11% to 29% since early 2000
- Absence of new antibiotics
  - Clinical failure in MDR (Multi-drug resistance)
  - Growing reliance on older and more toxic drugs (*e.g.* colistin)
  - No new class of Gram-negative small antibiotic has been produced in the last 50 years
- Two public workshops on non-traditional antibiotics held by DUKE university and the FDA in 2018

McKenna, National Geographic 2015

Antibody-based Anti-infective Therapies is NOT New

Emil Adolf von Behring

- The founder of serum therapy
- Discovery of diphtheria antitoxin serum in 1890 with Shibasaburo kitasato
- First to be honored by the Nobel Prize for Medicine in 1901

Box 1. **Indications for blood-derived antibodies for infectious diseases with a current American or European Union market authorization[a]**

- Anthrax: treatment of inhaled anthrax.
- Botulism: treatment of botulinum.
- *Clostridium botulinum*: treatment of infant botulism caused by type A or B *C botulinum* in patients < 1 year.
- Cytomegalovirus: prophylaxis of cytomegalovirus disease associated with transplantation of kidney, lung, liver, pancreas and heart.
- Diphtheria: treatment of diphtheria and rarely as prophylactic of diphtheria in asymptomatic, non-immunized individuals who have been exposed.
- Hepatitis A: protection from hepatitis A in household and other close contacts.
- Hepatitis B: prevention of Hepatitis B recurrence following liver transplantation; treatment of acute exposure to Hepatitis B-containing blood, sexual exposure to infected persons, infants born to infected mothers and household exposure to persons with acute infection.
- Hepatitis C: Prevention of recurrent hepatitis C virus-induced liver disease in liver transplant recipients.
- Measles: postexposure prophylaxis for suspected measles in unvaccinated persons.
- Rabies: postexposure prophylaxis to rabies category III exposure (i.e. single or multiple transdermal bites or scratches, contamination of mucous membrane with saliva from licks; exposure to bat bites or scratches).
- Rubella: prophylaxis of rubella to exposed individuals in early pregnancy.
- *Staphylococcus aureus*: treatment of *S aureus* bacteraemia.
- Tetanus: immediate prophylaxis after tetanus prone injuries in patients not adequately vaccinated, with unknown immunization status, severe deficiency in antibody production or vaccinated patients with high risk wounds.
- Vaccinia: prevention or treatment of vaccinia/smallpox. Treatment and/or modification of conditions which are complications resulting from smallpox vaccination.
- Varicella: prophylaxis against varicella zoster virus infection in at-risk exposed patients.

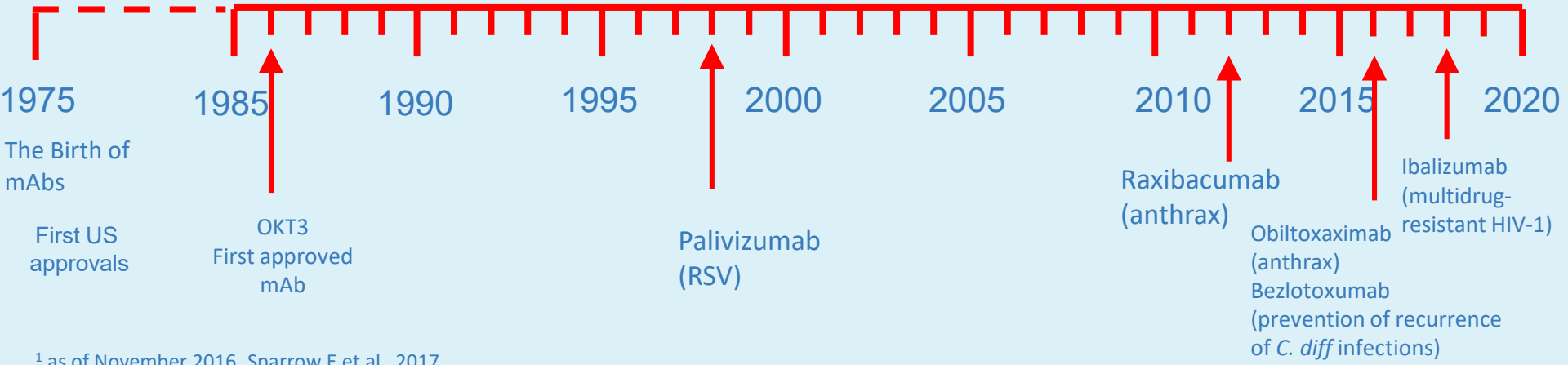
- Challenges
  - Standardization
    - Batch variability
  - Patient safety
    - Potential transmission of infectious hazards
  - Supply
  - Access
- Polyclonal antibodies from serum vs monoclonal antibodies

https://www.nobelprize.org/prizes/medicine/1901/behring/facts/

Sparrow E et al , 2017

Monoclonal Antibody for Infectious Disease

- There are five mAbs approved for infectious indications by the FDA to date
- At least 38 mAb products in active clinical development for 14 infectious diseases [1]



[1] as of November 2016, Sparrow E et al , 2017

Opportunities and Challenges for Monoclonal Antibodies for Infectious Diseases

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Opportunities

- Could have a wide range of biological targets (membrane protein, toxin, immune modulator and etc.)
- New modalities (antibody-antibiotics conjugates, bispecific Abs and etc.)
- Mitigate resistance threat
  - Targeting highly conserved epitopes
  - Using antibody cocktails containing multiple mAbs
  - A single product to target multiple pathogens
- Long half-life for prophylaxis and/or more convenience dosing regime for treatment

Challenges

- PK of mAbs may be different in patients vs healthy subjects
- PD biomarkers to support dose selection in Phase 2/3 studies
- Technical barriers
  - Target/biomarker selection
  - Rapid point-of-care of diagnostics
  - Meaningful translation from preclinical to clinical
- Pathogen escape
- Alternative regulatory pathways
  - Novel clinical study design

Sparrow E et al , 2017; Pelferne E et al 2019

Session Objectives

- Identify the opportunities and challenges in the development of antibody-based anti-infective therapies

- Initiate discussion about novel and feasible strategies to help solve the issues and accelerate the development process

Agenda

- Opening remark
  - Dr. Rong Deng (Genentech)
  - Dr. Yang He (Jaco Biopharmaceuticals)
- PK/PD challenges of developing Antibody-based anti-infective treatment
  - Dr. Joseph Balthasar (University at Buffalo –SUNY), 15 minutes
- A clinician's perspective – The opportunity and challenges of development of antibody-based anti-infective treatment
  - Dr. Joshua Galanter (Genentech), 15 minutes
- Experiences with development of antibody-based anti-viral drugs
  - Dr. Qin Sun (FDA), 15 minutes
- Opportunities and challenges in the development of monoclonal antibodies as an integrated and layered medical countermeasure
  - Dr. Jeffrey Froude (Defense Threat Reduction Agency, 15 minutes)
- Panel discussion (25 minutes)

Questions for Panel Discussion

- Is the concept of PKPD, similar to the small molecules anti-infective, suitable to support dose selection in the development of antibody-based anti-infective? If not, what strategy should we use for dose selection?
  - Depending on MOA
  - Meaningful translation from preclinical to clinical
  - PK and /or PK/PD at site of action
  - PK in healthy volunteers vs patients
- Clinical study design
  - Patient population selection
  - Meaningful clinical endpoints
- Scientific, regulatory and economic barriers