

Novartis Adjuvanted Trivalent Influenza Virus Vaccine (aTIV)

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Head, Development

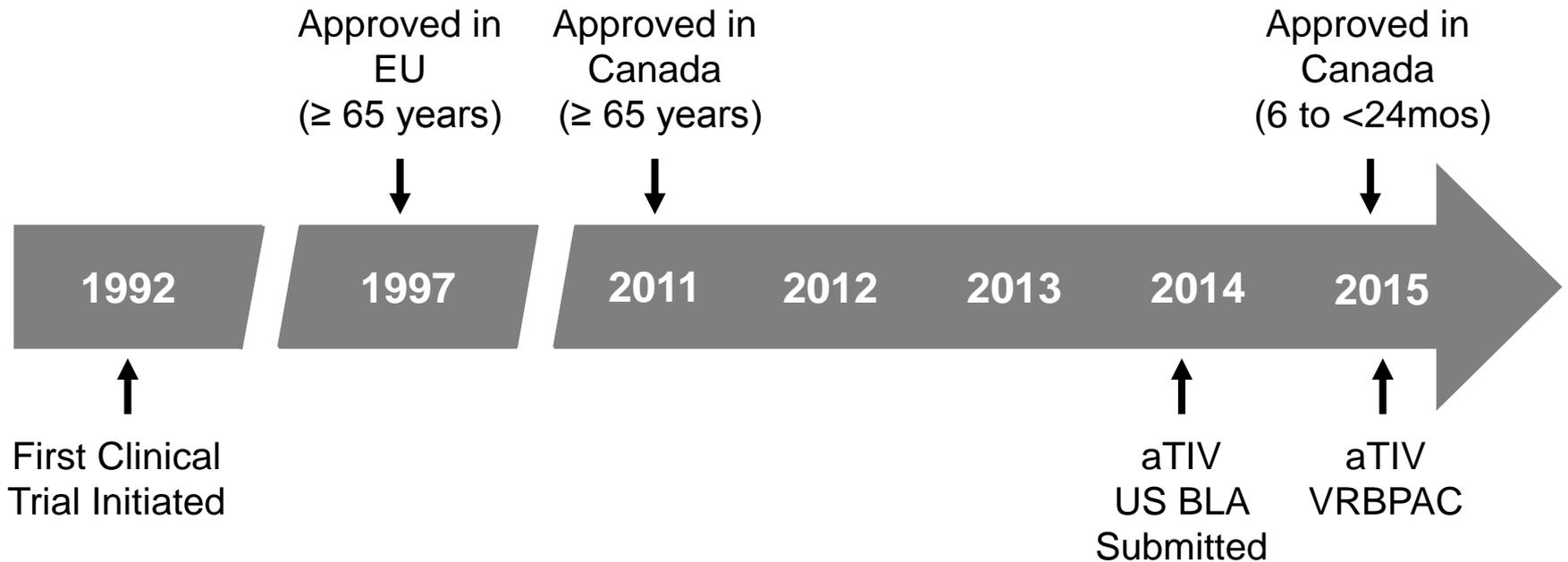
NVS Influenza Vaccines

October 21, 2015

Agenda

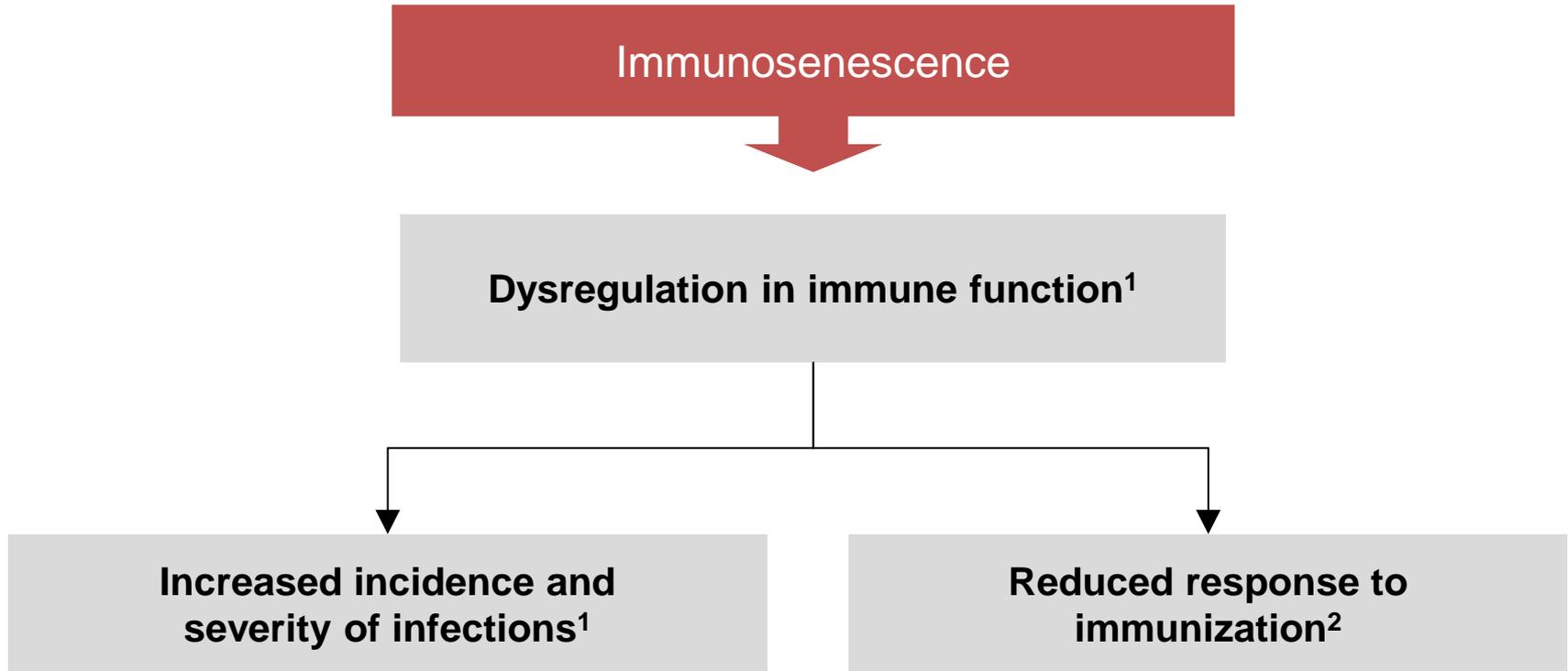
- Overview of aTIV Development
- MF59 Mechanism of Action
- Immunogenicity
- Safety Profile
- Effectiveness: Observational Studies

Timeline of aTIV Experience



- Approved in >30 countries
- >76 million doses distributed

Immunosenescence: Aging of Immune System



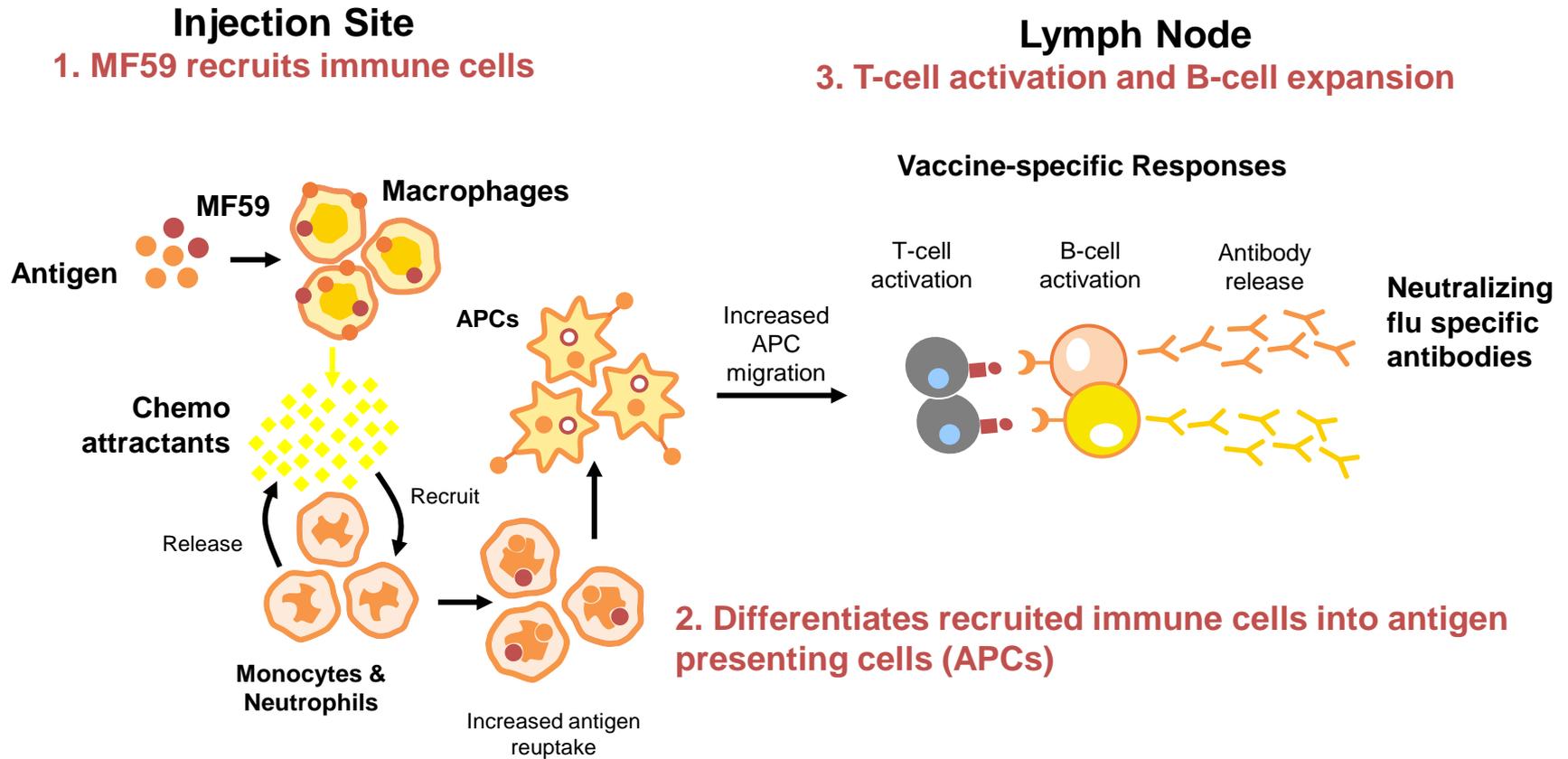
1. Kumar R, Burns EA., Expert Rev Vaccines, 2008.

2. High K., Clin Geriatr Med, 2007.

MF59: Adjuvant Component of aTIV

- Enhances immune response
- Maintains acceptable safety profile
- MF59 adjuvant contains:
 - Squalene
 - Surfactants
 - Citrate

MF59 Mode of Action at Injection Site



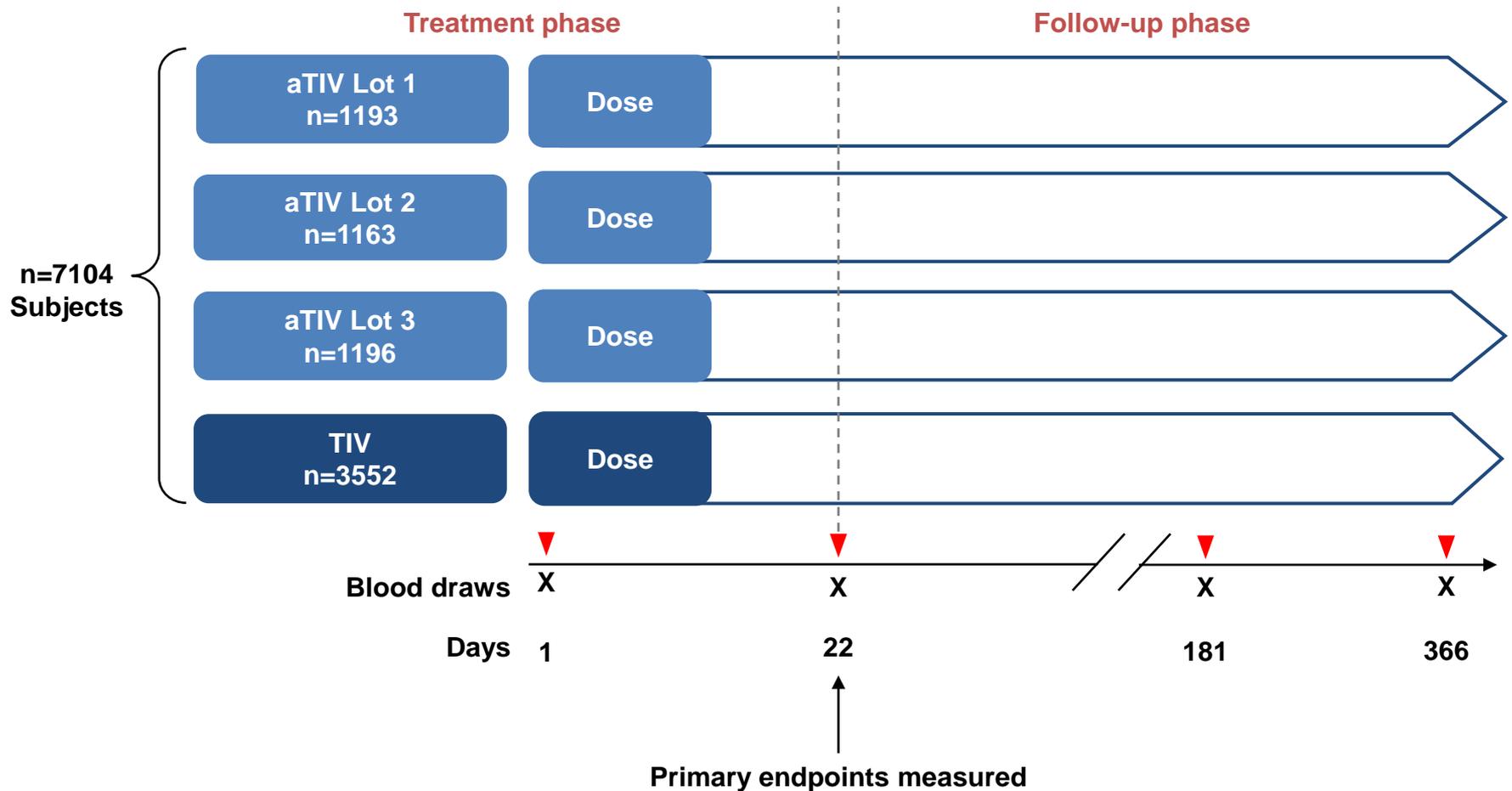
Seubert et al., J Immunol, 2008; Schultze et al., Vaccine, 2008.
Khurana et al., Sci Transl Med, 2010.
Calabro et al., Vaccine, 2011.
Vono et al., Proc Natl Acad Sci USA, 2013.

Clinical Program Supports Benefits of aTIV in Older Adults

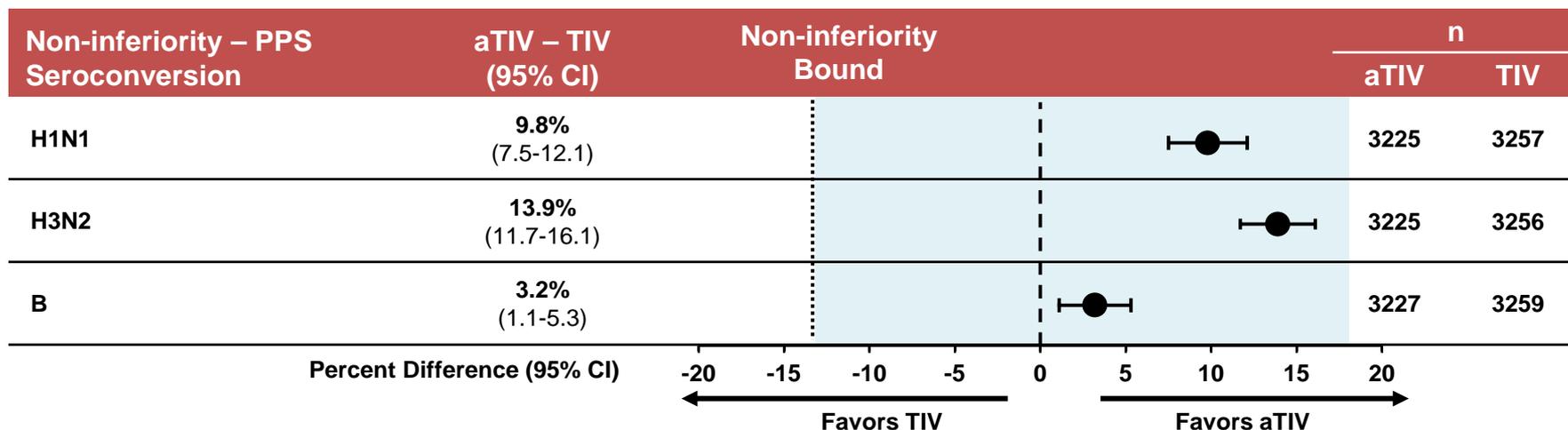
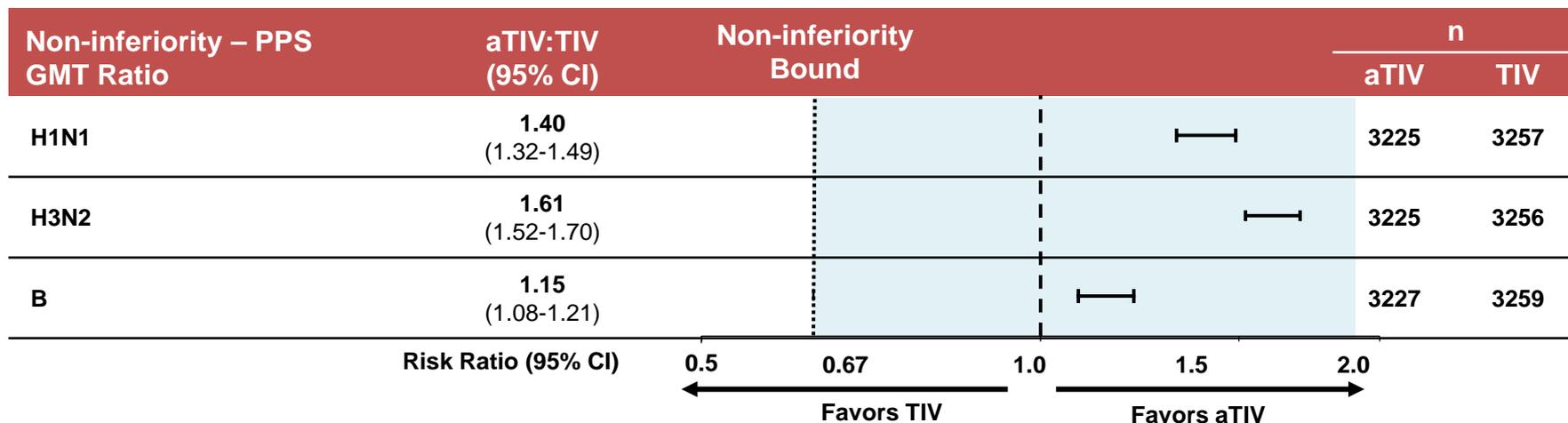
- 39 interventional clinical trials in older adults (n >27,000 individuals)
 - 16 open-label studies
 - 23 randomized clinical trials
 - 16 first-dose studies
 - Pivotal study (V70_27)
 - 7 revaccination trials
 - 5 trials with 2nd dose
 - 2 trials with 3rd dose
- 2 observational studies

Pivotal Study: Study Design

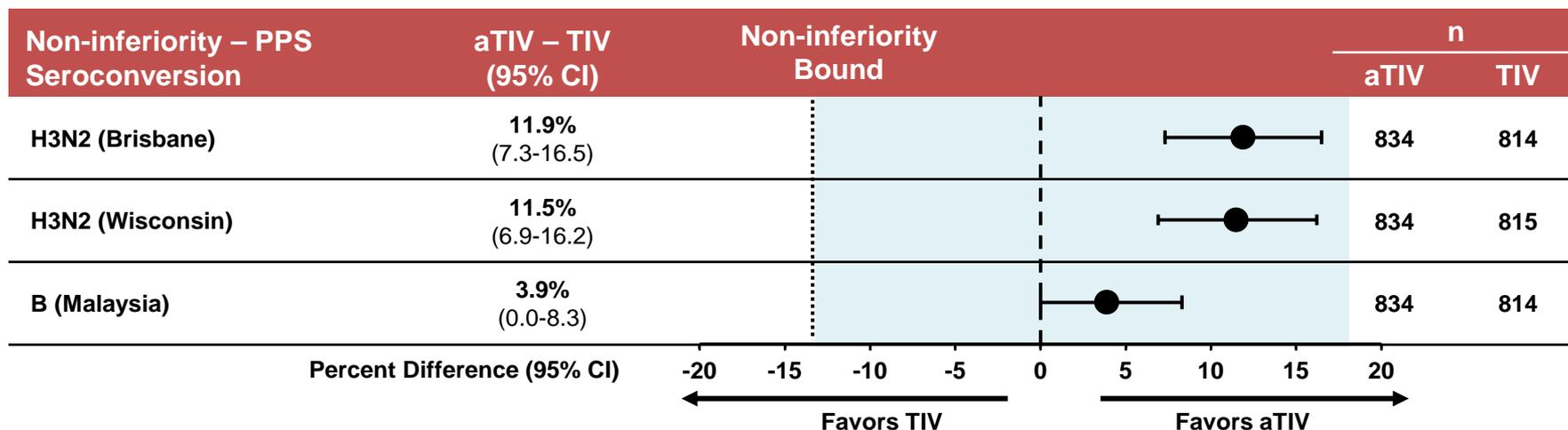
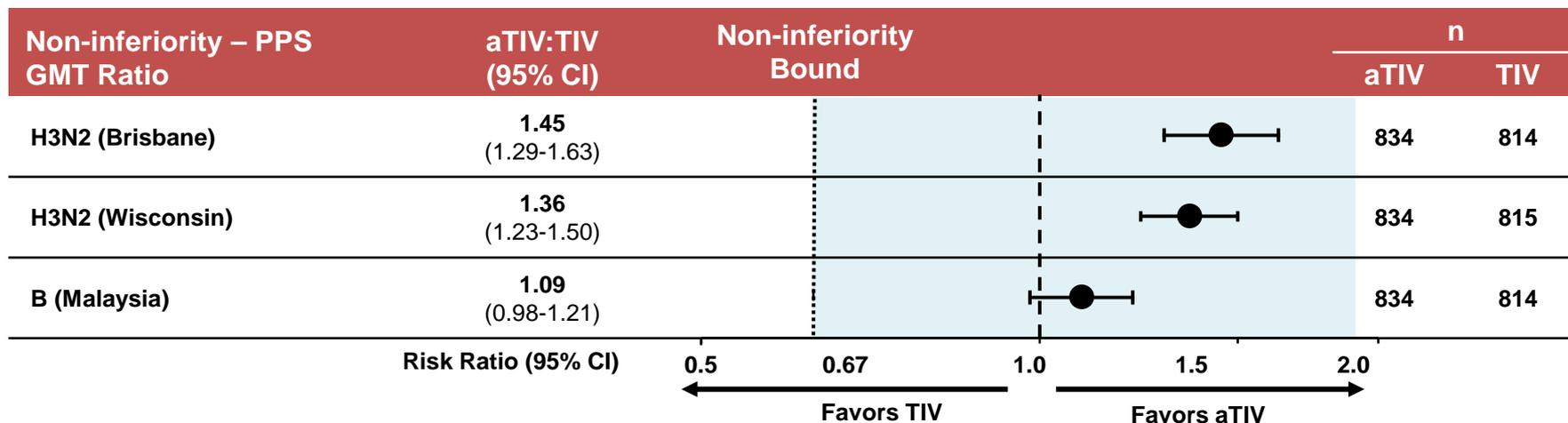
Immunogenicity and Safety Trial



aTIV Demonstrated Non-Inferiority for GMT and Seroconversion



aTIV Met Non-Inferiority Criteria for Heterologous Strains

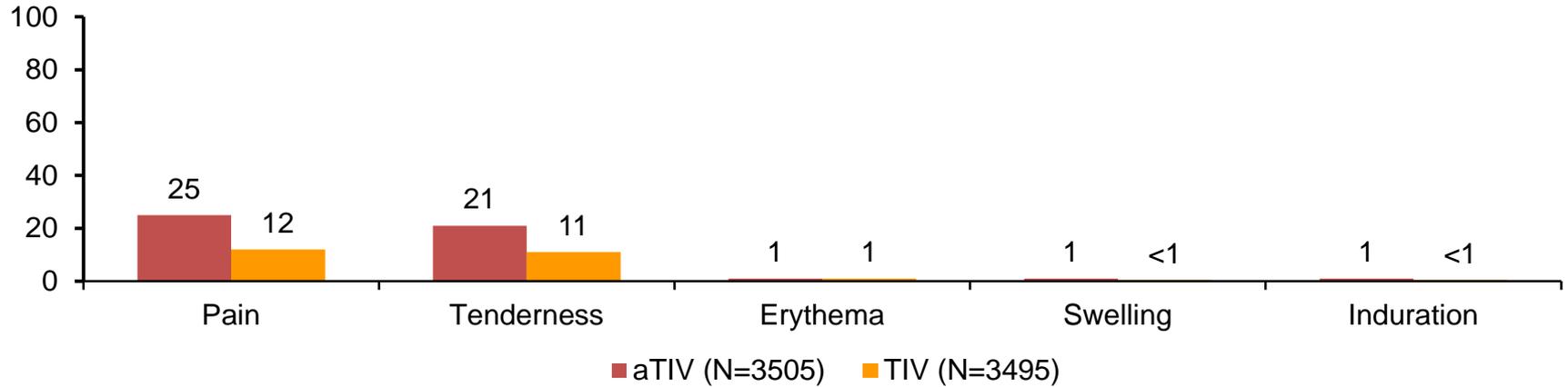


Pivotal Study: Safety Profile of aTIV and TIV

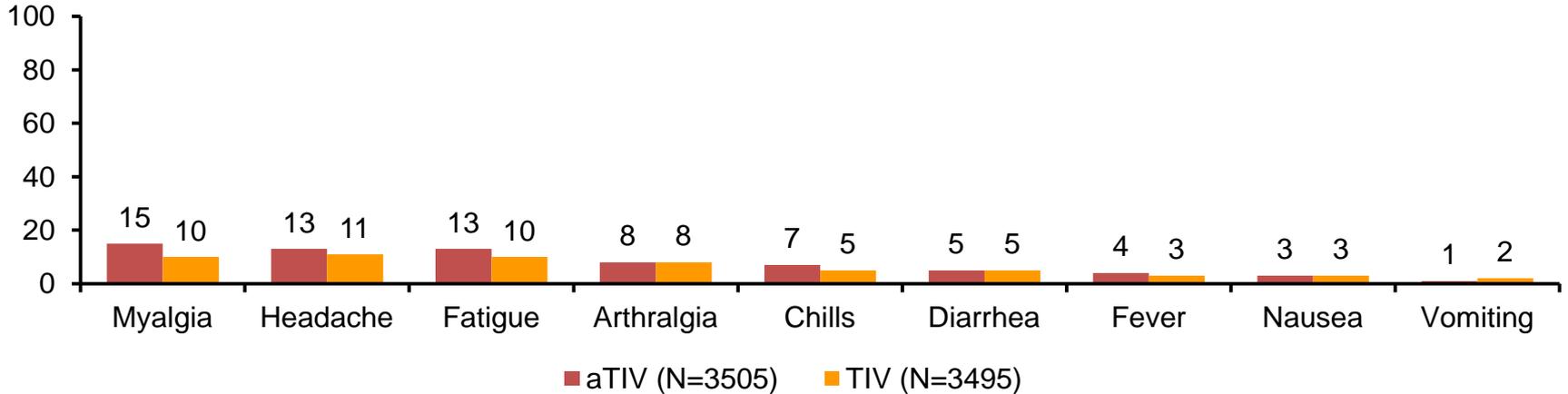
Subjects with at least one event	Assessment Period	aTIV N=3545	TIV N=3537
Death	Day 1-366	1.5%	1.3%
SAEs		7%	7%
AEs leading to withdrawal		1%	1%
Unsolicited AEs	Day 1-22	16%	16%
		N=3515	N=3502
Solicited AEs	Day 1-7	46%	33%

Pivotal Study: Overall Solicited AEs

Subjects (%)



Subjects (%)



Days 1-7 following vaccination

Post-Marketing Data

- 17 years of clinical use, >76 million doses distributed
- Routine surveillance and customized searches
 - No novel safety signals observed
 - No narcolepsy cases identified
- Targeted analysis
 - Adverse Events of Special Interest (AESI)
 - Adverse Events Following Immunization (AEFI)

Effectiveness Study #1: Lombardia Influenza Vaccine Effectiveness (LIVE) Study

- Large community-based observational study
- aTIV recipients at baseline:
 - More comorbidities
 - Higher functional impairment
 - More likely to be hospitalized
- aTIV recipients showed 25% risk reduction in hospitalization for influenza and pneumonia

Manino et al., Am J Epidemiol., 2012.

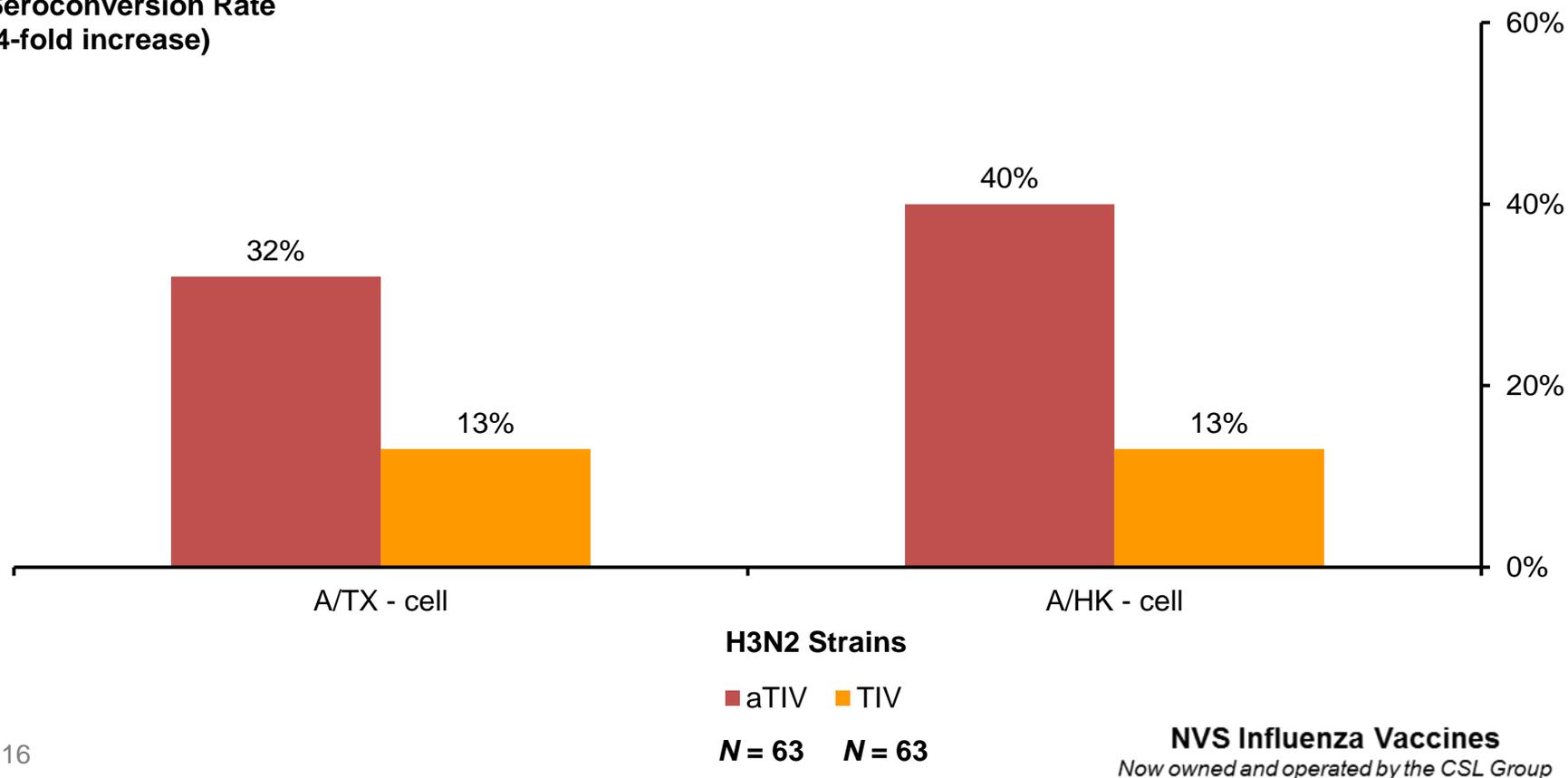
Effectiveness Study #2: Canadian Comparative Study

- Case-control test negative, community-based study in British Columbia
- aTIV recipients at baseline
 - More co-morbidities
 - More often over 85 years of age
 - More often resident in long-term care facilities,
- In older patients with co-morbidities, 63% vaccine effectiveness of aTIV vs. TIV in this H3N2-predominate season

aTIV Expands Serologic Coverage of 14/15 NH H3N2 Mismatch

Adjuvanted vaccine generated a higher percentage of significant titer increase against both matched (A/Texas) and mismatched (A/Hong Kong) strains

**Microneutralization
Titers
Seroconversion Rate
(4-fold increase)**



aTIV Overall Summary

- aTIV generated higher antibody titers
- aTIV well-tolerated, acceptable safety profile similar to other licensed vaccines
- aTIV demonstrated consistent enhanced effectiveness in LIVE and Canada Comparativeness study
- aTIV demonstrated higher immune responses to drifted strains in the 2014-2015 influenza season