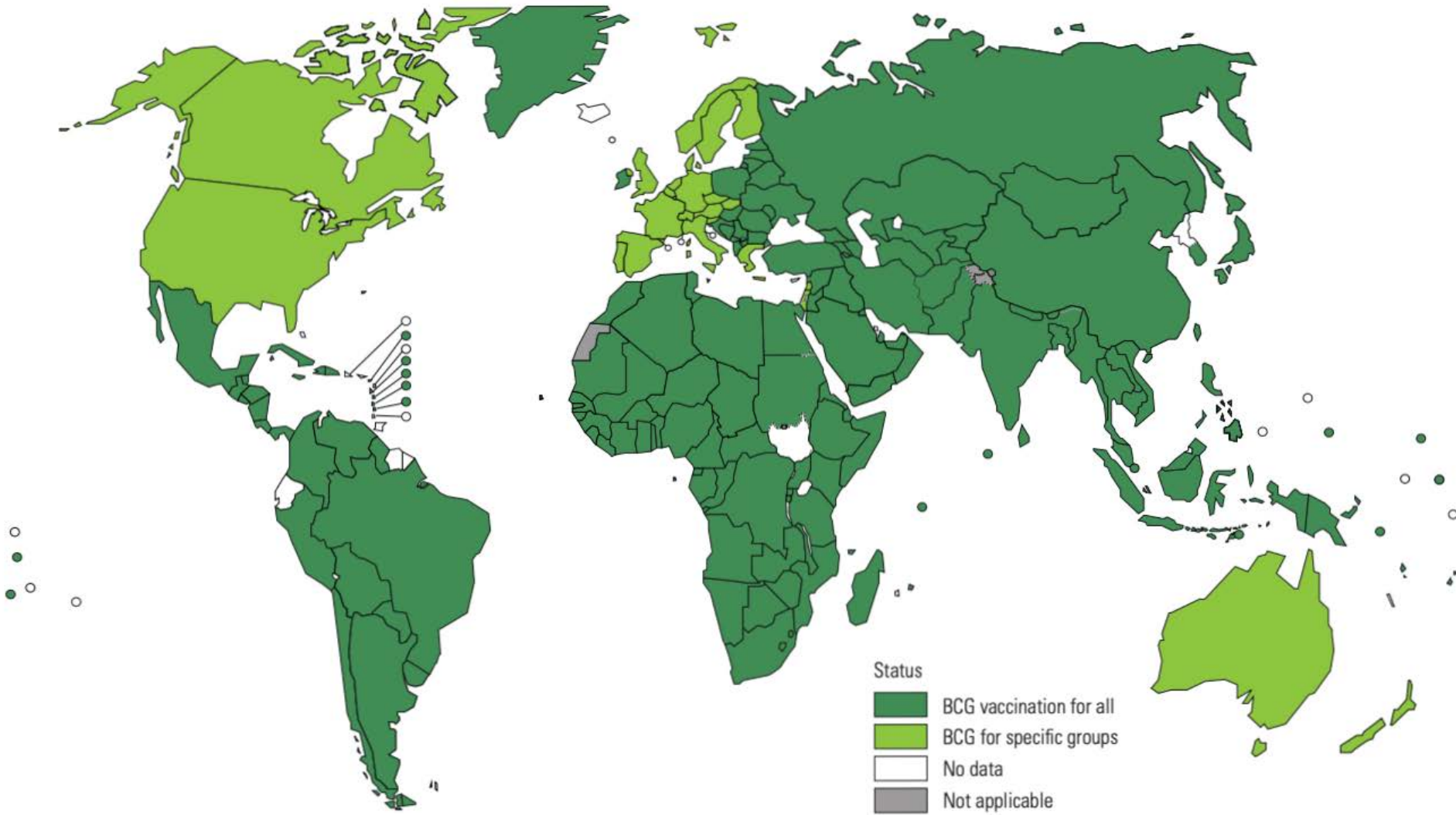


The importance of BCG strain
differences in determining bladder
cancer efficacy

Global Burden

- In 2019,
 - 10 million new cases of Tb
 - 1.2 million TB deaths among HIV neg
 - 0.2 million TB deaths among HIV-pos
- Bacille Calmette-Guérin (BCG) – only available vaccine
 - Protects (>80% efficacy) against **severe** Tb (meningitis and miliary) in children
 - Adolescents and Adults: variable efficacy

BCG vaccination practices by country



Source: The BCG World Atlas 2nd Edition, <http://www.bcgatlas.org/>, accessed August 2020

Global Burden

- Historically,
 - BCG strains considered to possess ‘equivalent’ vaccine properties
 - Only one BCG strain usually selected for vaccine studies
- Advances in genomics and understanding of virulence mechanisms of *M. tb* - re-evaluate assumptions about strain differences

Conclusions

- BCG strains differ genetically
- Are their strain differences?
- Do strains have differences in efficacy?

BCG: History



Albert Calmette
(1863-1933)



Camille Guérin
(1872-1961)



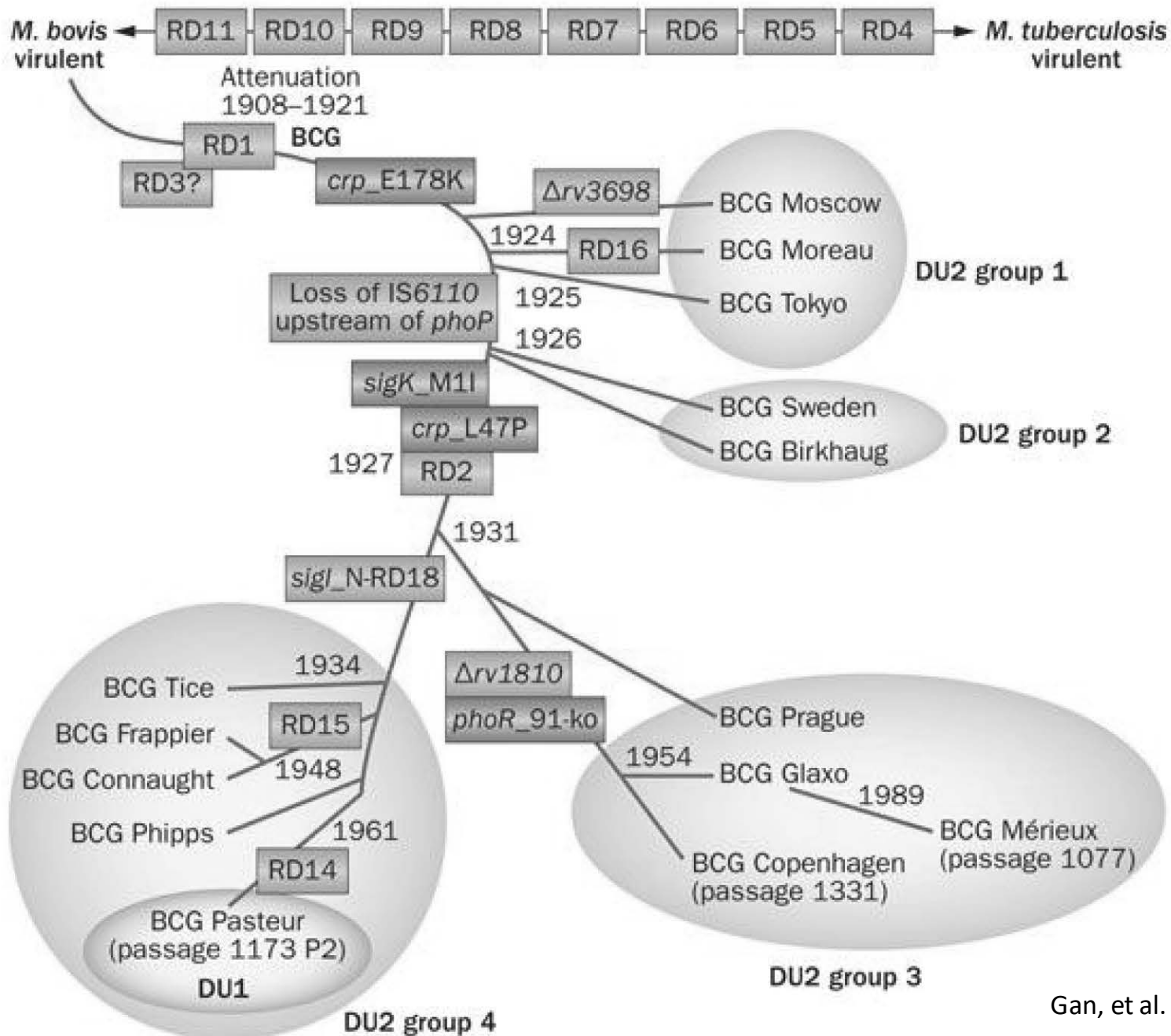
History of BCG vaccine

- Timeline
 - “Lait de Nocard” – *M. bovis* isolated from cow with Tb mastitits
 - 1908-Pasteur Institute (Calmette and Guerin)
 - 1915-Cows then guinea pigs
 - **1921- First** administered to baby
 - 1921-1924- 217 Paris children
 - 1924 – Mass production began

In vitro evolution of BCG

- Despite efforts to standardize the growth and preparation of the vaccine, different passaging conditions were used in different production laboratories
- Dozens of distinct daughter strains emerged:
 - BCG-Pasteur
 - BCG-Japan (Tokyo-172)
 - BCG-Danish (Copenhagen-1331)
 - BCG-Glaxo

Genealogy of BCG strains



BCG strains in TB Efficacy

- 5-10% of infected individuals develop active TB disease
- Correlates of protection not available
- Head-to-head trials not been done

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European Association of Urology



Platinum Priority – Bladder Cancer

Editorial by XXX on pp. x–y of this issue

Bacillus Calmette-Guérin Strain Differences Have an Impact on Clinical Outcome in Bladder Cancer Immunotherapy

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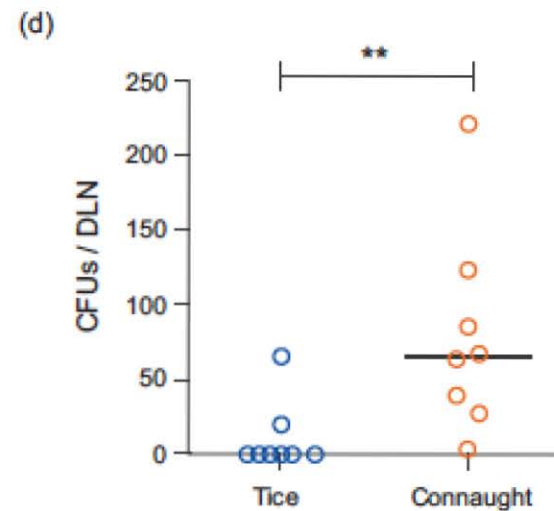
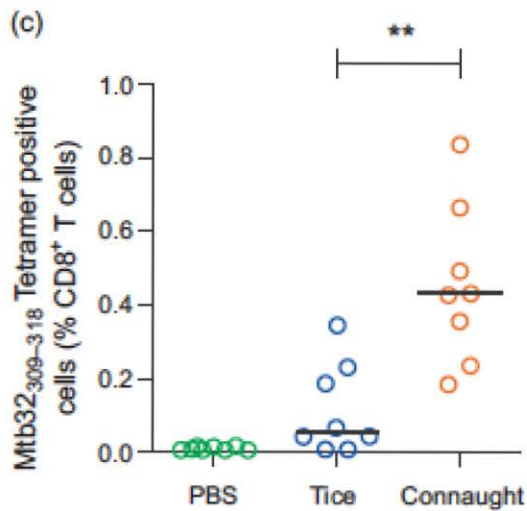
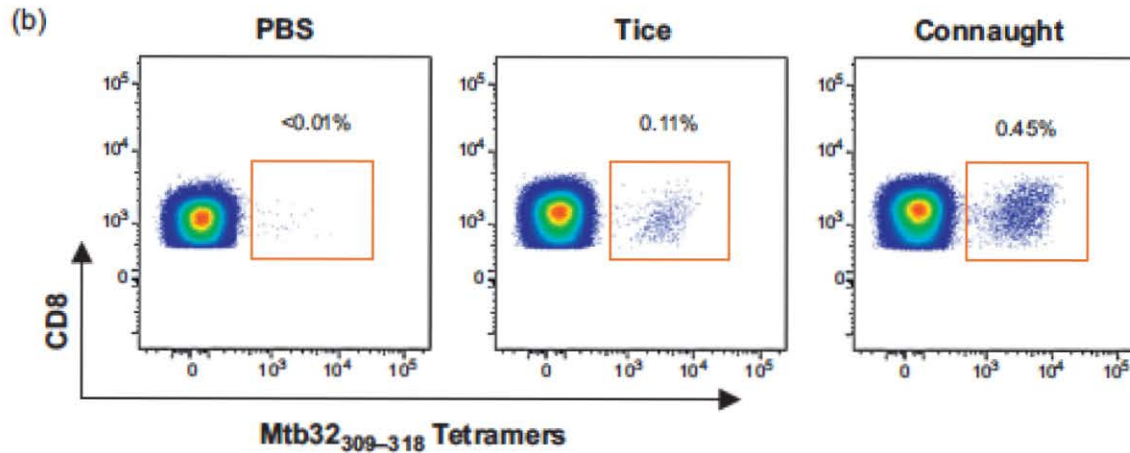
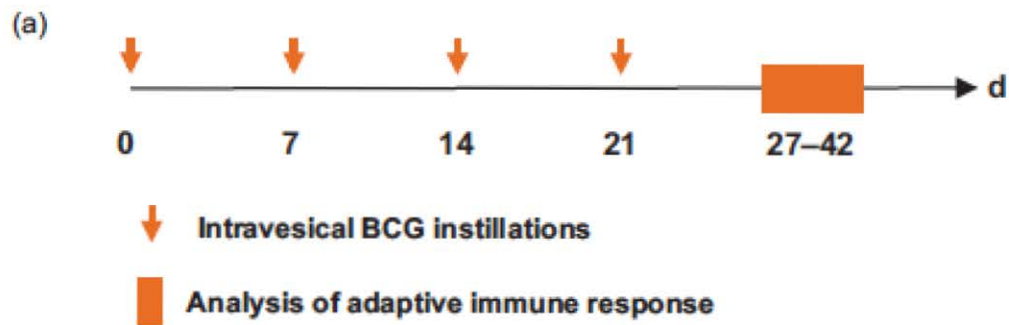
Urinary bladder neoplasms
BCG vaccine

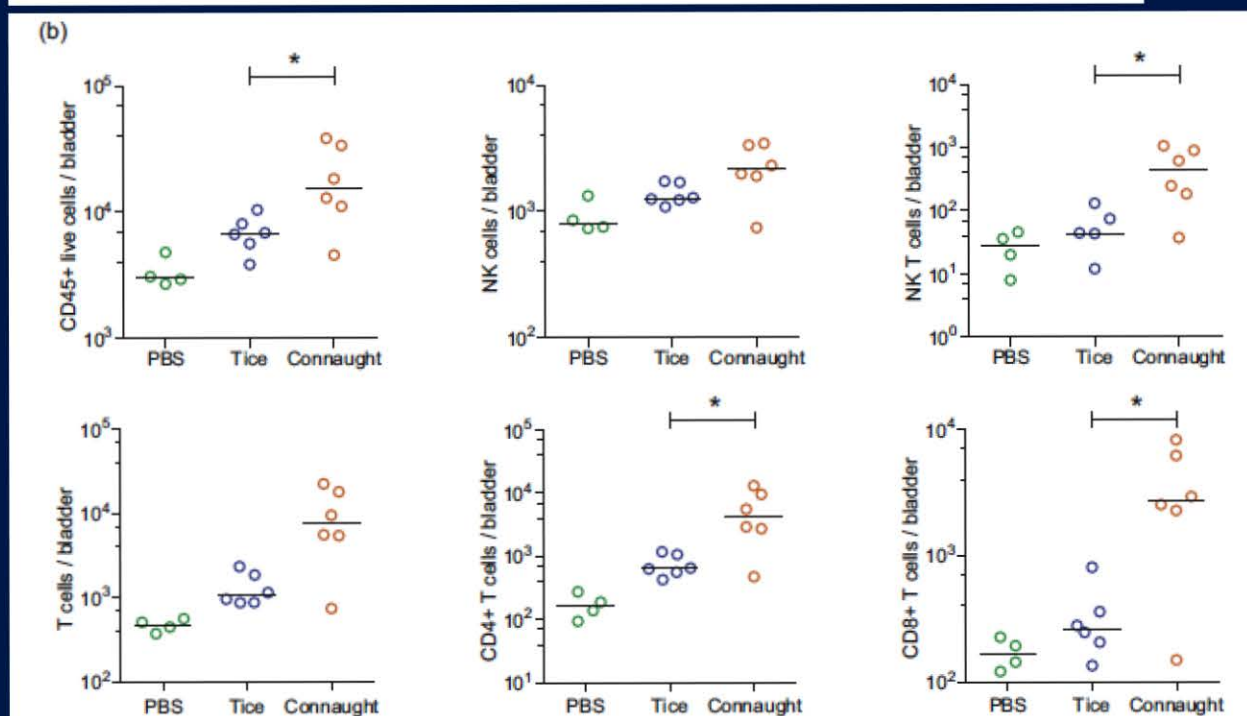
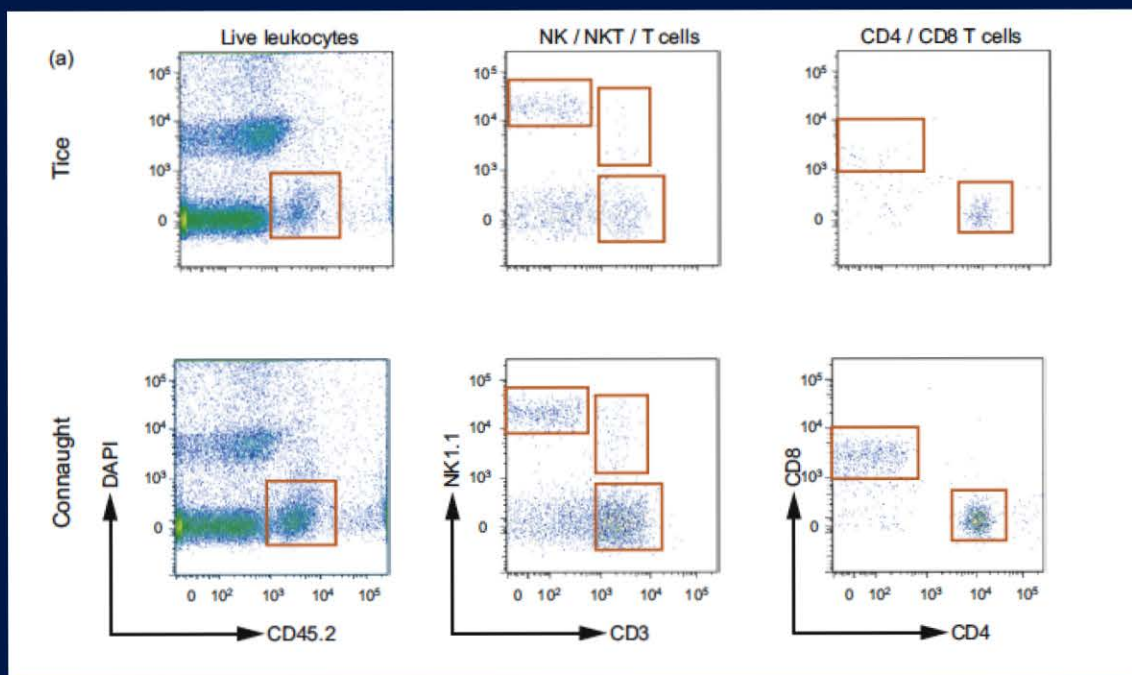
Abstract

Background: Whether the commonly used bacillus Calmette-Guérin (BCG) strains Connaught and Tice confer different treatment responses in non-muscle-invasive bladder cancer (NMIBC) is unknown.

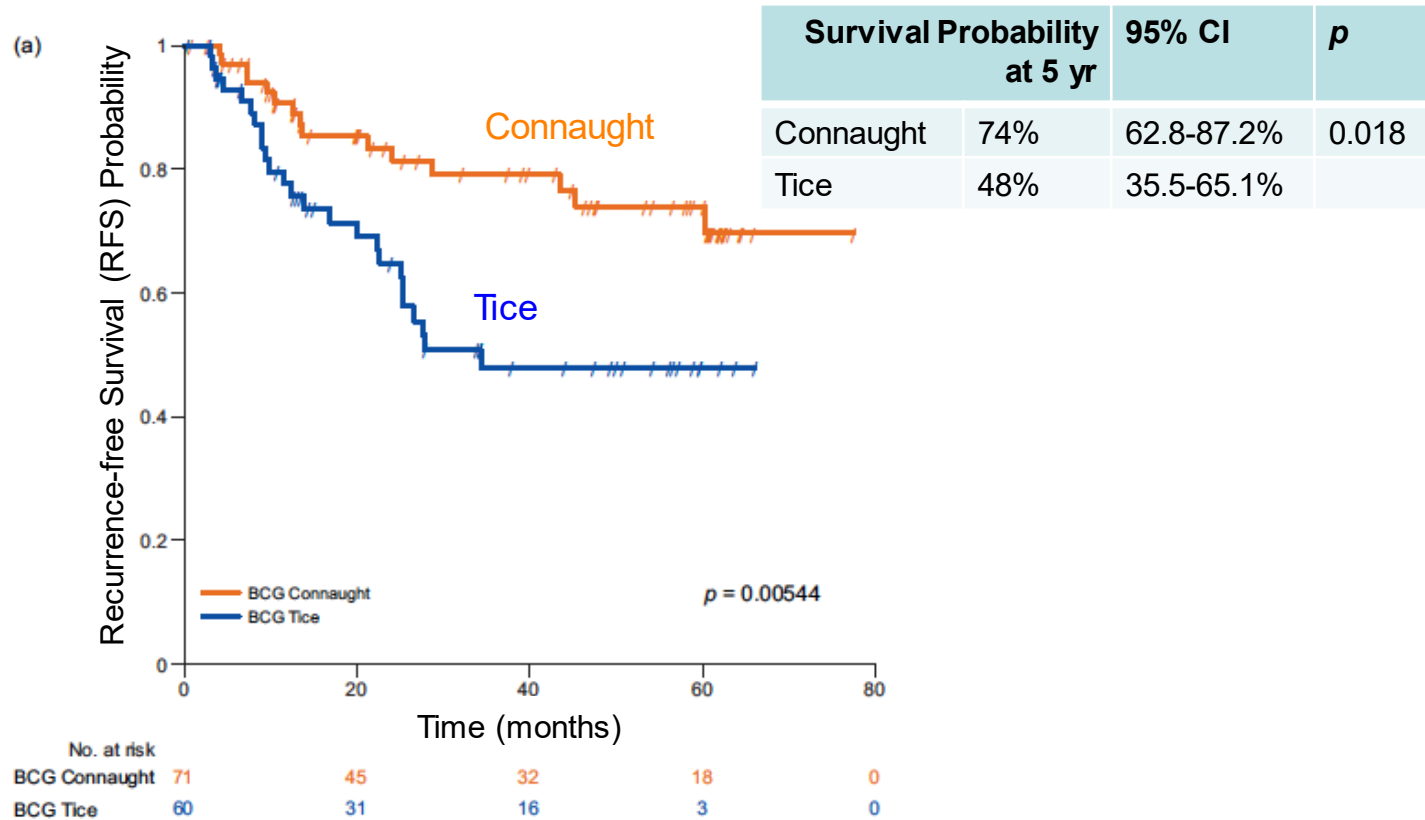
Objectives: To compare clinical efficacy, immunogenicity, and genetics of BCG Connaught and Tice.
Design, setting, and participants: A prospective randomized single-institution trial with treatment of 142 high-risk NMIBC patients with BCG Connaught or Tice.

Intervention: Patients were randomized to receive six instillations of BCG Connaught or Tice. For experimental studies, BCG strains were compared in C57Bl/6 mice. Bladders and lymphoid tissues were analyzed by cytometry and the latter cultivated to detect live BCG. BCG genomic DNA was sequenced and compared with reference sequences.



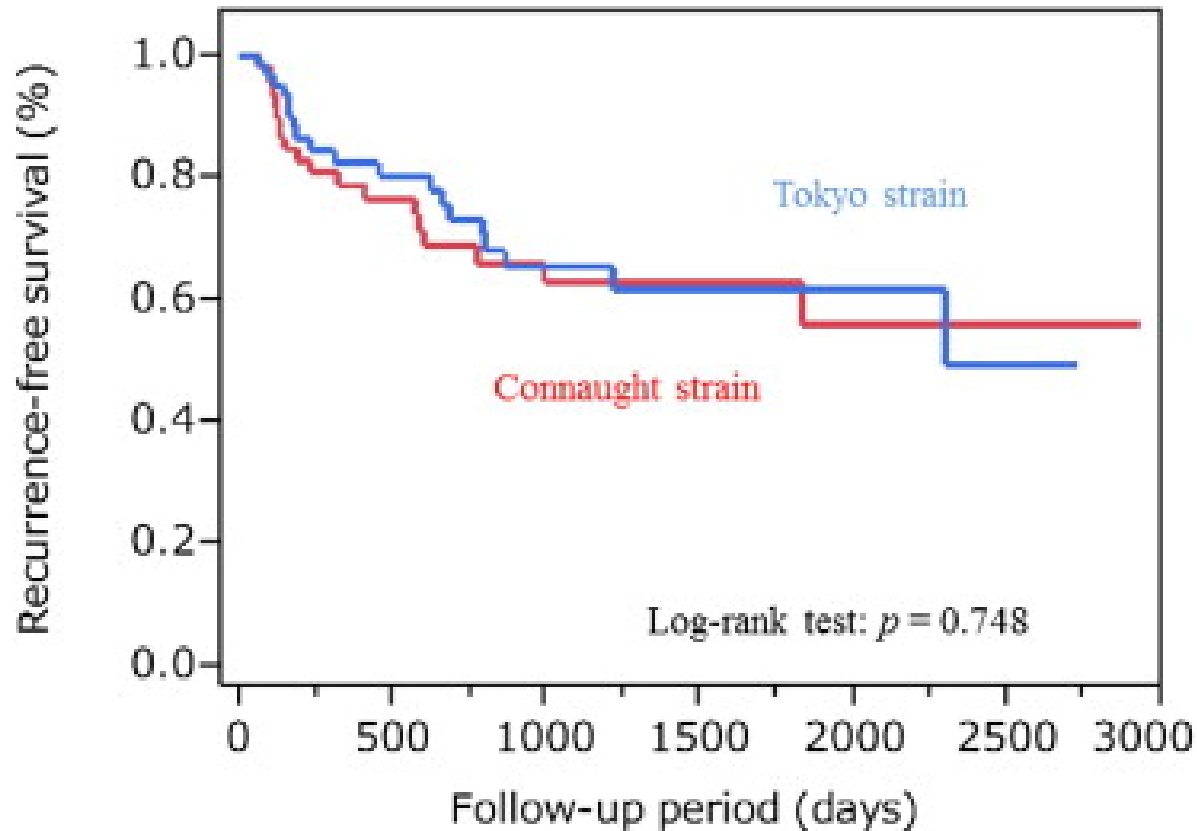


Are some BCG strains better than others?



A Prospective Comparative Study of Intravesical Bacillus Calmette-Guérin Therapy with the Tokyo or Connaught Strain for Nonmuscle Invasive Bladder Cancer

Atsushi Sengiku, Masaaki Ito, Yu Miyazaki, Harutake Sawazaki, Takeshi Takahashi, Keiji Ogura



S1602 Trial Schema

