Kolmas annos immuunipuutteisille?

Valituja ACIP 13.8.2021 dioja

https://www.cdc.gov/vaccines/acip/meetings/slides-2021-08-13.html

Immunocompromised People and SARS-CoV-2 Infection

- Immunocompromised people comprise ~2.7% of U.S. adults (~7 million adults)[1]
- More likely to get severely ill from COVID-19[1,2]
- Higher risk for:
  - Prolonged SARS-CoV-2 infection and shedding[3-7, 14-16]
  - Viral evolution during infection and treatment (hospitalized patients)[3,6,8-10,14,17]
- Lower antibody/neutralization titers to SARS-CoV-2 variants compared to non-immunocompromised people [12]
- More likely to transmit SARS-CoV-2 to household contacts[11]

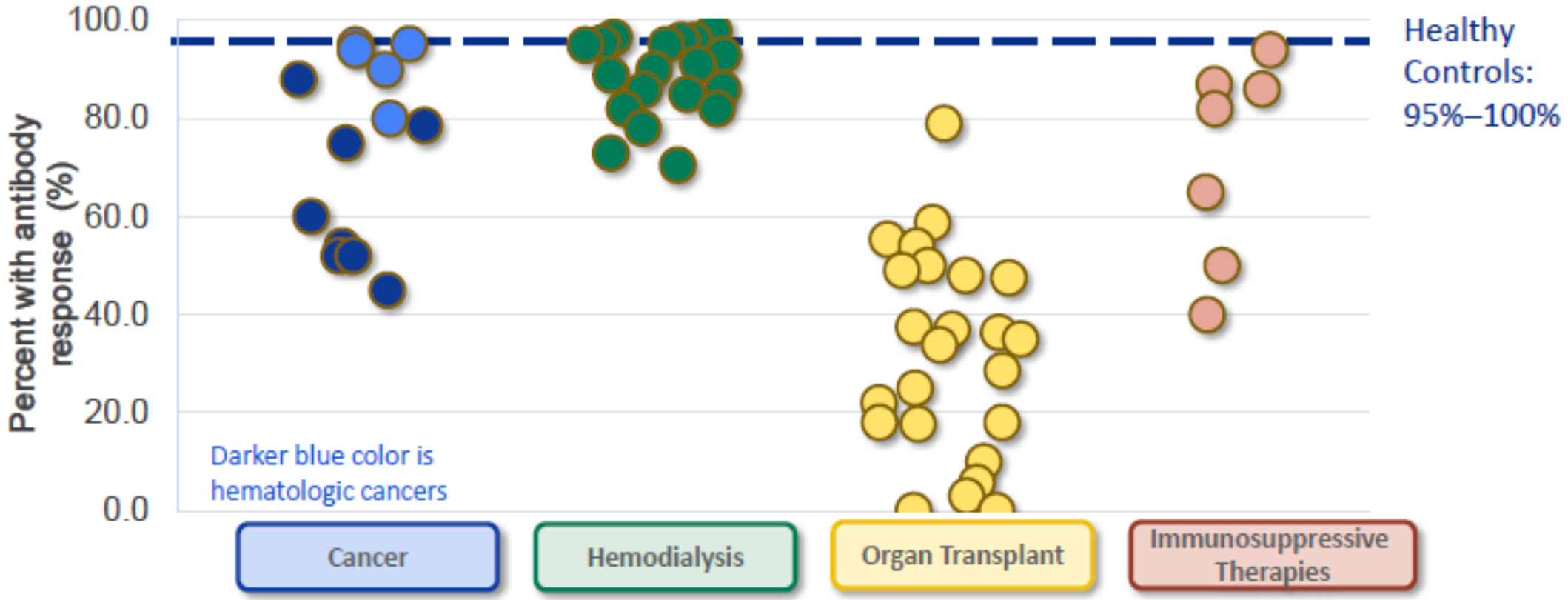
See reference slide at end

Immunocompromised People and Vaccine Breakthrough Infection

- More likely to have breakthrough infection
  - 40-44% of hospitalized breakthrough cases are immunocompromised people in US study[1-2]
- Lower vaccine effectiveness
  - 59--72% VE among immunocompromised people vs. 90--94% among non-immunocompromised people after 2nd dose[1, 3-5]

See reference slide at end

Percent of subjects with antibody response after two mRNA COVID-19 vaccine doses by immunocompromising condition and study (n=63)

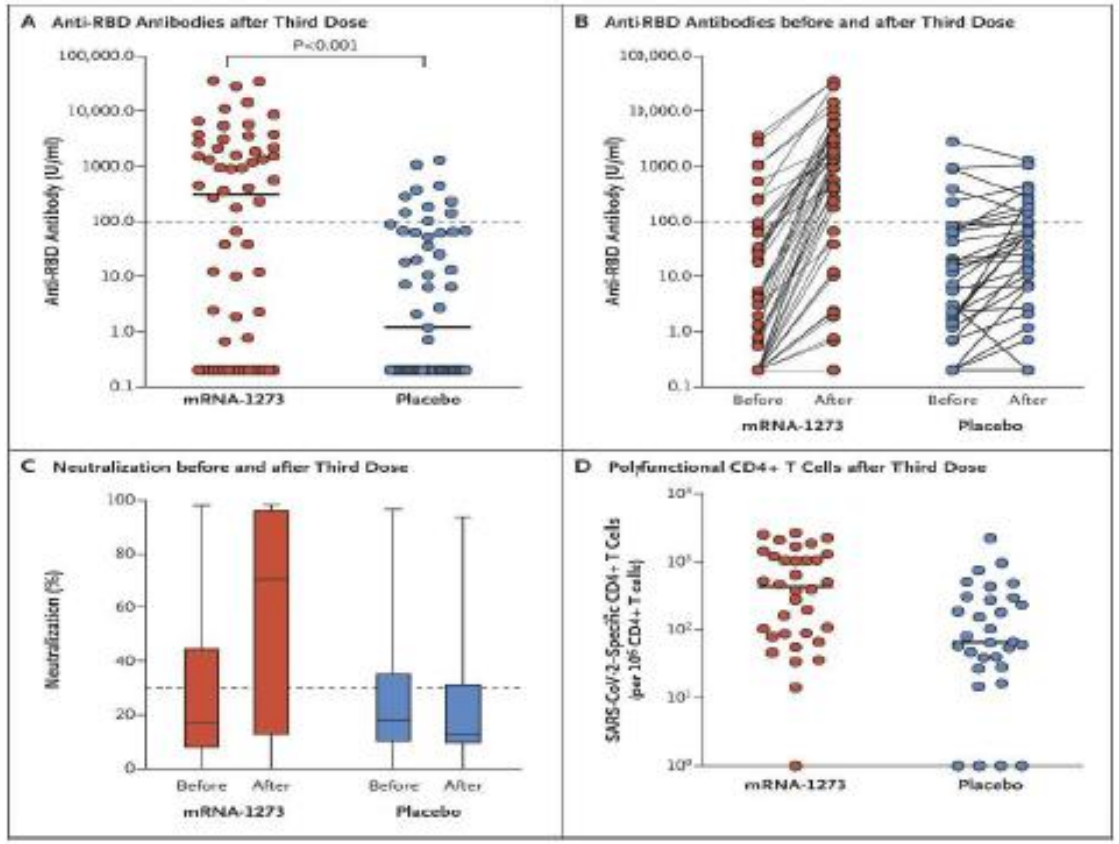


- Studies that compared response after 1st and 2nd dose demonstrated less robust response after dose 1
- Antibody measurement and threshold levels vary by study protocol

See reference slide at end

Benefits:

Randomized Trial of a 3rd Dose of Moderna Vaccine in Transplant Recipients (n=120)



RBD antibody (≥100 U/ml)
1 month post dose 3:

33 of 60 patients
(55%) vaccine group
vs.
10 of 57 patients
(18%) placebo group

Hall et al. (2021) NEJM. Randomized Trial of a Third Dose of mRNA-1273 Vaccine in Transplant Recipients. DOI: 10.1056/NEJMc2111462

Benefits:

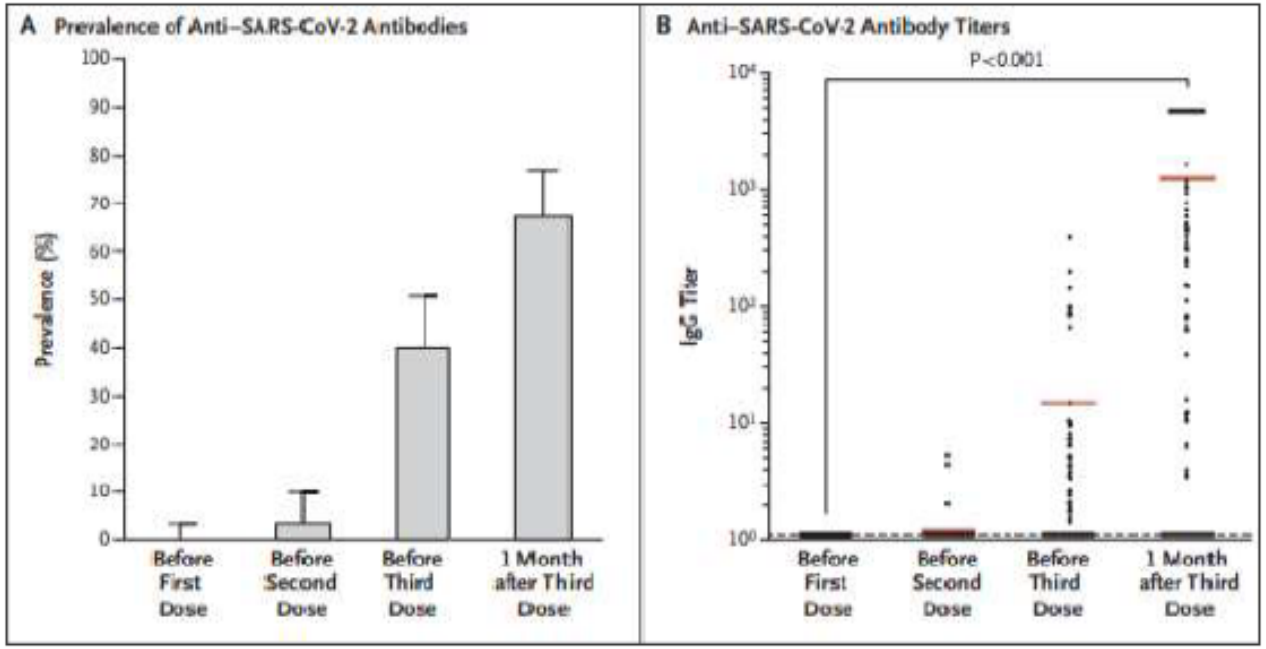
Study	Patient Population	2nd Dose			3rd Dose Seronegative after 2 nd dose		
		Sample Size	Seronegative N (%)	Seropositive N (%)	Sample Size	Seronegative N (%)	Seropositive N (%)
Kamar et al.	Recipients of solid-organ transplant	99	59 (60)	40 (40)	59	33 (56)	**26 (44)**
Werbel et al.	Recipients of solid-organ transplant	30	24 (80)	6 (20)	24	16 (67)	**8 (33)**
Longlune et al.	Patients on hemodialysis	82	13 (16)	69 (84)	12	7 (58)	**5 (42)**
Epsiet al.	Patients on hemodialysis	106	66 (62)	40 (38)	12	6 (50)	**6 (50)**
Ducloux et al.	Patients on hemodialysis	45	5 (11)	40 (89)	5	3 (60)	**2 (40)**

- Among those who had **no detectable antibody** response to an initial mRNA vaccine series,

33-50% developed an antibody response to an additional dose

See reference slide at end

Benefits and Harms:

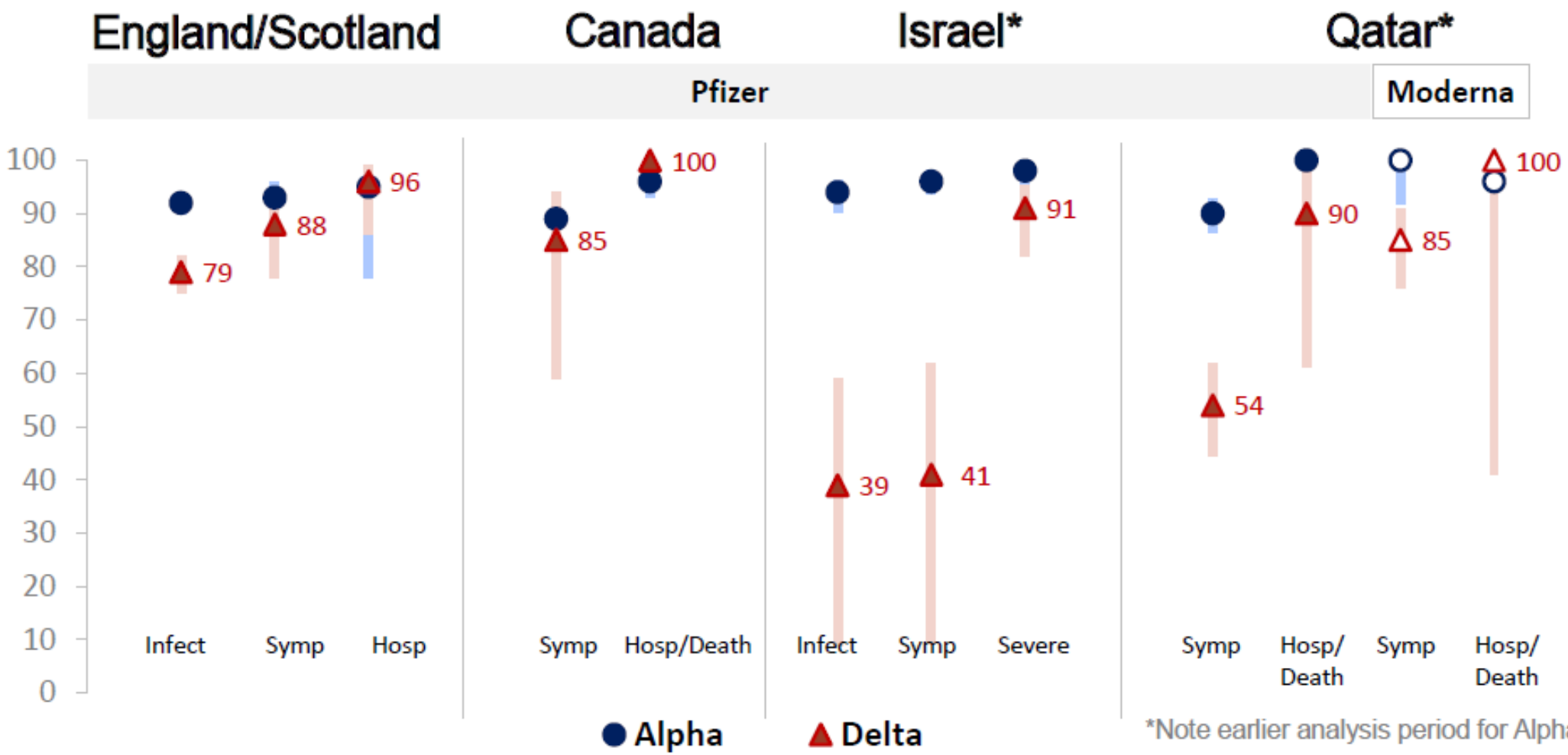


- The proportion of the group who are seropositive increase after each dose: **40%** post dose 2 and **68%** post dose 3
- Average antibody titre increased after each dose
- No serious adverse events were reported after administration of the 3rd dose, and no acute rejection episodes occurred (n=99 Solid Organ Transplant Patients)

Kamar et al. (2021) NEJM Three Doses of an mRNA Covid-19 Vaccine in Solid-Organ Transplant Recipients (nejm.org)

EtR Domain	Question	Work Group Judgments
Public Health Problem	Is COVID-19 disease among immunocompromised people of public health importance?	**Yes**
Benefits and Harms	How substantial are the desirable anticipated effects?	**Large**
	How substantial are the undesirable anticipated effects?	**Minimal**
	Do the desirable effects outweigh the undesirable effects?	**Favors additional dose of mRNA vaccine in immunocompromised people**
	What is the overall certainty of the evidence for the critical outcomes?	**Not GRADED**
Values	Does the target population feel the desirable effects are large relative to the undesirable effects?	**Large**
	Is there important variability in how patients value the outcomes?	**Probably not important variability**
Acceptability	Is an additional dose of mRNA COVID-19 vaccines acceptable to key stakeholders?	**Yes**
Feasibility	Is an additional dose of mRNA COVID-19 vaccine feasible to implement among immunocompromised people?	**Yes**
Resource Use	Is an additional dose of mRNA COVID-19 vaccine, given to immunocompromised people, a reasonable and efficient allocation of resources?	**Yes**
Equity	What would be the impact of an additional dose of mRNA COVID-19 vaccine, given to immunocompromised people, on health equity?	**Probably no impact**

Pfizer & Moderna 2-Dose Effectiveness for Alpha vs. Delta



*Note earlier analysis period for Alpha vs Delta

Sheikh et al. Lancet (2021): https://doi.org/10.1016/S0140-6736(21)01358-1; Lopez Bernal et al. medRxiv preprint; https://doi.org/10.1101/2021.05.22.21257658; Stowe et al. PHE preprint: https://khub.net/web/phe-national/public-library/-/document_library/v2WsRK3ZlEig/view/479607266; Nasreen et al medRxiv preprint: https://doi.org/10.1101/2021.06.28.21259420; Haas et al Lancet (2021): https://doi.org/10.1016/S0140-6736(21)00947-8 ; Israel MOH: https://www.gov.il/BlobFolder/reports/vaccine-efficacy-safety-follow-up-committee/he/files_publications_corona_two-dose-vaccination-data.pdf Abu-Radad and Butt, NEJM (2021); Chemaitelly et al. Nature Med (2021); Tang et al medRxiv

Differences in COVID vaccination program by country with potential impact on comparability of VE results

Country	U.S.	Israel	Qatar	U.K.	Canada
Vaccines used [authorized]	Pfizer Moderna Janssen	Pfizer [Moderna]	Pfizer Moderna	Pfizer AstraZeneca [Moderna] [Janssen]	Pfizer Moderna AstraZeneca [Janssen]
Interval	3-4 weeks	3 weeks	3-4 weeks	12 weeks	16 weeks
Note	-	Tight cohort	-	Mix-and-match	

- Extended intervals between doses (12 weeks) shown to improve immunogenicity and VE for Pfizer and AstraZenaca vaccines compared with standard interval, including ages ≥80 years
- Pfizer has lower mRNA dosage and accelerated schedule (3 weeks) compared with Moderna (4 weeks)

Parry et al. https://www.medrxiv.org/content/10.1101/2021.05.15.21257017v1 ; Flaxman et al. Lancet (2021) https://papers.ssrn.com/sol3/papers.cfm?abstract_id=3873839 ; Amirthalingam et al. https://www.medrxiv.org/content/10.1101/2021.07.26.21261140v1; Carazo et al. : https://doi.org/10.1101/2021.07.19.21260445

References: Immunocompromised people and SARS-CoV-2 infection (Slides 15)

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2. Brosh –Nissimiv et al. *BNT162b2 vaccine breakthrough: clinical characteristics of 152 fully-vaccinated hospitalized COVID-19 patients in Israel* (2021) https://doi.org/10.1016/j.cmi.2021.06.03
3. Chodick G et al. The Effectiveness of the Two-Dose BNT162b2 Vaccine: Analysis of Real-World Data. Clinical Infectious Diseases, ciab438. https://doi.org/10.1093/cid/ciab438;
4. Khan N, Mahmud N. Effectiveness of SARS-CoV-2 Vaccination in a Veterans Affairs Cohort of Patients With Inflammatory Bowel Disease With Diverse Exposure to Immunosuppressive Medications. Gastroenterology(2021). https://www.gastrojournal.org/article/S0016-5085(21)03066-3/pdf
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