


Vakcinace dětí s imunodeficiency

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věnuje hlavně dětem s výraznými imunodeficity, dětem po transplantaci hematopoetických buněk a solidních orgánů.

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Riziko preventabilních infekcí u dětí po transplantaci hematopoetických buněk

Burden of Vaccine-Preventable Infections (VPI) in HCTr

- Pediatric Health Information System (PHIS) 2010-2018
- 684/9,591 (7.1%) children had a VPI-associated hospitalization in the first 5 years after HCT
- Risk factors for VPI: PIDD (OR 1.78), GVHD (OR 1.62), young age (OR 0.96)

Table 4. Outcomes of vaccine preventable infections hospitalization in children after hematopoietic cell transplantation, multivariate analysis by time post-transplant.

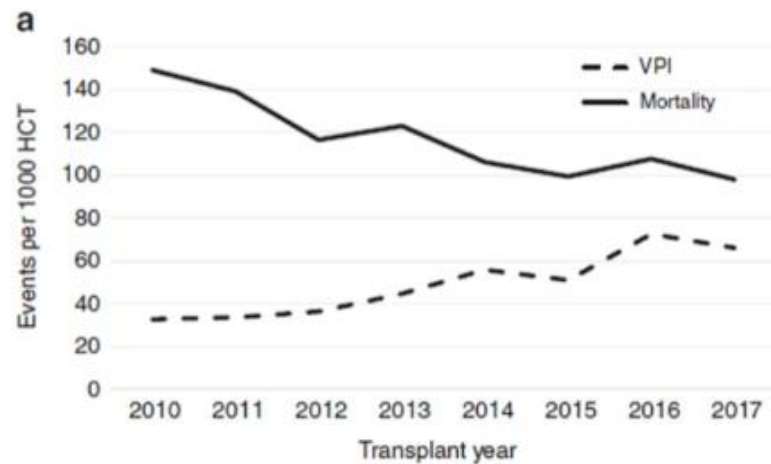
Variables	HCT with VPI	HCT no VPI	p value
Duration of hospitalization median (IQR)	55 (51)	36 (24)	<0.0001
ICU admit n (%)	65 (42)	2453 (26)	<0.0001
Mechanical ventilation n (%)	37 (24)	1056 (11)	<0.0001
Mortality n (%)	17 (11)	517 (5)	0.003

Danino et al, TCT BMT, 2019

- 9leté období
- 9 591 dětí s HCTr
- 684 (7,1 %) rozvinulo vakcínou preventabilní onemocnění v prvních 5 letech
- Dominovaly: IPO, chřipka, neštovice

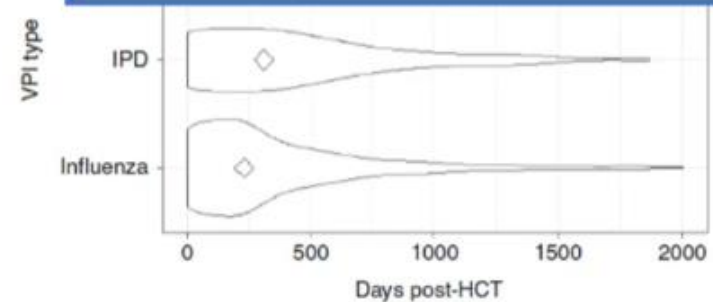
Riziko preventabilních infekcí u dětí po transplantaci hematopoetických buněk

Burden of Vaccine-Preventable Infections (VPI) in HCTr



b

VPI occurred most frequently in the first 6-12 months post-HCT



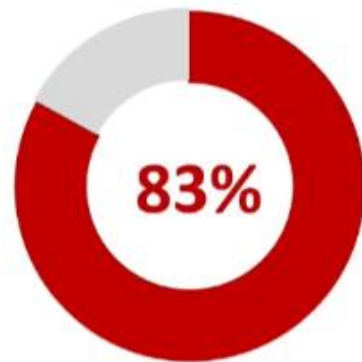
Riziko preventabilních nemocí u dětí po transplantaci solidních orgánů

Burden of VPI in SOTr

- Pediatric Health Information System (PHIS) 2004-2011
 - 1,092/6,980 (15.6%) SOTr were hospitalized with a VPI in the first 5 years after SOT ~ 87-fold higher rate of VPI-hospitalization than general population
 - Influenza, varicella, pneumococcus, rotavirus
 - VPI-related case fatality rate of 1.7% ~ 17x ↑ pneumococcal mortality rate than general population
 - VPI-associated hospitalizations were longer and cost median \$120,498 USD more than non-VPI transplant hospitalizations
- 8leté období
 - 6 980 transplantací
 - 1 092 dětí rozvinulo vakcínou preventabilní infekci (15,6 %)

Proočkovanost pacientů po transplantaci hematopoetických buněk

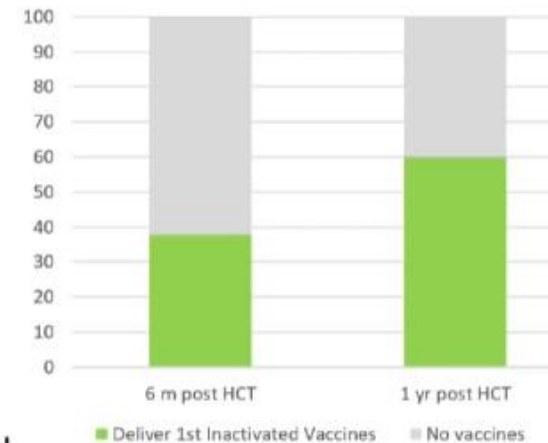
Suboptimal Immunization Practices after HCT: Recipients Remain at Risk for VPI



Pediatric HCT recipients with IPD were unimmunized or incompletely immunized



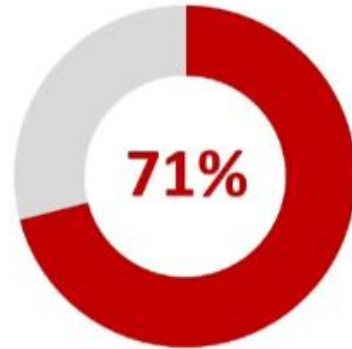
Pediatric HCT centers in National Marrow Donor Program follow CDC recommendations to vaccinate 3-6 months after HCT



Non-live vaccine delivery among HCT recipients

Proočkovanost pacientů po transplantaci solidních orgánů

Under-Immunization of SOT Candidates: Children Remain at Risk for VPI



Pediatric candidates across
US Liver Transplant Centers
were NOT up-to-date on
age-appropriate vaccines

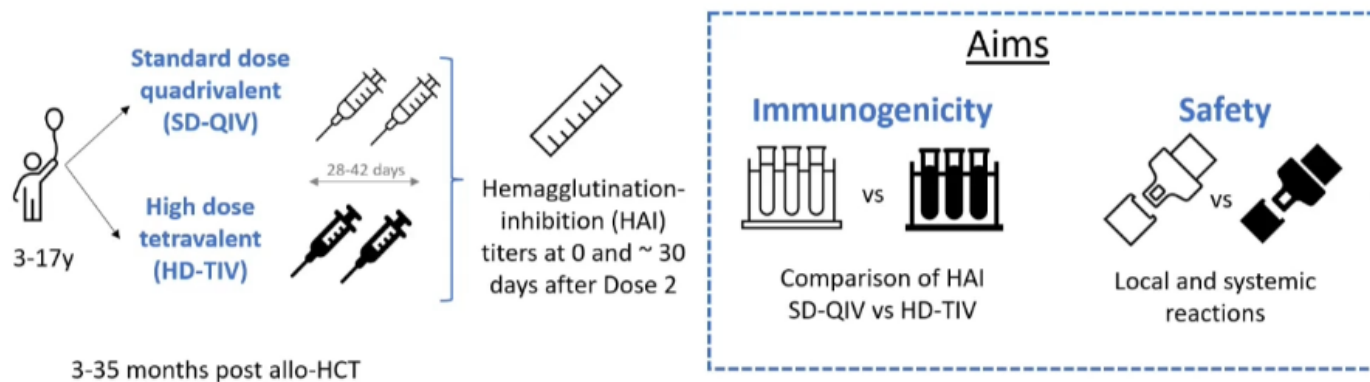
Vaccines provided pre-SOT:

- are more immunogenic
- ↑ immunogenicity of vaccines given post-SOT

Vakcinace proti chřipce

Optimizing Inactivated Influenza Vaccine (IIV) after allo-HCT

- Phase 2, nine center, double-blind, RCT among 170 pediatric allo-HCTr over 3 influenza seasons (2016-2019)



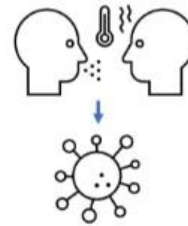
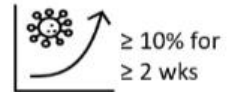
- Pacienti po transplantaci – větší riziko závažného průběhu i úmrtí chřipky
- Nižší protilátková odpověď
- Vysokodávková vakcína s vyšším množstvím antigenu k dispozici pouze pro dospělé (60+)
- Studie u dětí po HCT

Výsledky

- Signifikantně vyšší titry protilátek po aplikaci 2 dávek vysokodávkové vakcíny (HD-TIV) se stejným bezpečnostním profilem
- NU: po HD-TIV vyšší výskyt lokálních reakcí v místě vpichu po 2. dávce vakcíny
- Závažné nebo systémové NU byly srovnatelné po aplikaci obou vakcín

Laboratory-Confirmed Influenza

- Active influenza surveillance during influenza season
- Flu testing: at each study visit and if influenza-like illness (ILI)



13 subjects + Influenza PCR
6 SD-QIV
3 HD-TIV

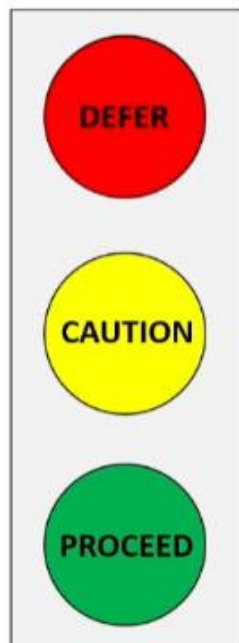
Year	Vaccination Group	Months Post-HCT at First Vaccination	Strain	Months from Dose 1 to Infection	Months from Dose 2 to Infection
1	SD-QIV	18.4	A/H3N2	4.3	2.7
1	SD-QIV	15.5	B/Victoria	4.9	3.8
1	HD-TIV	4.1	B/Yamagata*	3.6	2.4
2	SD-QIV	7.3	A/H3N2	2.8	1.0
2	HD-TIV	3.6	B/Yamagata*	1.2	0.2
2	HD-TIV	12.0	B/Yamagata*	2.7	1.3
2	SD-QIV	11.4	B/Yamagata	5.4	4.2
2	HD-TIV	5.5	A/H3N2	5.3	4.1
2	HD-TIV	20.0	B/Yamagata*	4.7	3.3
3	HD-TIV	7.6	A/Untypable	2.9	1.8
3	HD-TIV	9.2	A/H3N2	6.1	5.0
3	SD-QIV	6.3	A/H1N1	4.4	3.3
3	SD-QIV	6.4	A/H3N2	4.9	2.4

* B/Yamagata is not included in HD-TIV.

Očkování živými vakcínami

ORIGINAL ARTICLE

Live vaccines after pediatric solid organ transplant: Proceedings of a consensus meeting, 2018



- Clinically unwell, active infections, or rejection (ACR, AMR)
- Cardiac, lung, or multivisceral transplant or underlying PIDD
- High IST: Prednisone > 2 mg/kg/day; Tacrolimus \geq 8 ng/mL, cyclosporine \geq 100 ng/mL; ATG or rituximab within 12 months; alemtuzumab within 24 months

- Receipt of MMF; Receipt of ATG within 24 months
- Persistently elevated EBV viral loads
- Complete thymectomy during neonatal period
- Liver recipients in clinical tolerance

- Liver and kidney transplants,
- \geq 1 year post SOT AND \geq 2 months post ACR treatment, and
- Min immunosuppression (Tacro < 8, cyclosporine < 100, prednisone < 2 mg/kg/day),
- Meet minimum immune criteria

Vakcinace proti VZV a MMR po transplantaci

PROCEED

Proceeding with VZV & MMR post-SOT

min. lymfocytů
více: než 1500 u
dětí do 6 let
a 1000 u dětí nad
6 let
CD4: více než
700 u dětí do 6
let věku, a více
než 500 u dětí
nad 6 let

- Minimal immune evaluation
 - Absolute lymphocyte count (ALC)
 - Absolute CD4
 - Total IgG
- Potential indications to vaccinate:
 - Higher prevalence area
 - Travel to endemic area
 - Outbreak scenarios
- Consider starting with VZV

Minimum Immune Criteria:

- ALC
 - >1500 for children ≤6 y and >1000 cells/μL for children >6 y
- CD4
 - >700 cells/μL for children ≤6 y and >500 cells/μL for children >6 y
- Normal total serum IgG for age

- If active and passive surveillance mechanisms are in place
- If process exists to evaluate concerns (fever, rash) and test
- ± Informed consent obtained

Imunogenita vakcín proti VZV a MMR u pacientů po transplantaci

Vaccine Immunogenicity post-SOT: 72-99%

Table 2. Immunologic Response to Pretransplant and Posttransplant Live Viral Vaccines

Time of immunologic assessment	No./total No. (%) with protective titers			
	Varicella	Measles	Mumps	Rubella
After first posttransplant vaccine ^c	53/116 (46)	92/129 (71)	62/101 (61)	100/106 (94)
After second posttransplant vaccine ^c	61/81 (75)	48/60 (80)	41/52 (79)	43/44 (98)
After third posttransplant vaccine ^c	5/9 (56)	3/6 (50)	5/6 (83)	5/5 (100)
After final posttransplant vaccine ^c	107/149 (72)	130/152 (86)	100/120 (83)	124/125 (99)
1 y Postvaccine ^d	34/44 (77)	45/49 (92)	35/42 (83)	51/54 (94)

Bezpečnost očkování živými vakcínami u pacientů po transplantaci

Safety

- No serious adverse events
- Varicella rash = 5 patients
 - Reported ≥ 7 days post vaccine
 - Resolved within 1 week, 3 received antivirals
 - All were receiving moderate or high-level immunosuppression
- Subauricular lymph node swelling in 1 patient, not mumps
- No measles
- No rubella
- No episodes of acute cellular rejection within 1 month post vaccination

Závěr

- Snaha o adekvátní vakcinaci imunosuprimovaných dětí.
- Neoddalovat zbytečně očkování a nevystavovat děti zbytečně riziku infekce se závažnými průběhy.
- I živé vakcíny lze bezpečně aplikovat.