EE390

OPTIMISING THE USE OF RISK FACTORS TO GUIDE THE COST-EFFECTIVE USE OF PALIVIZUMAB PROPHYLAXIS AGAINST SEVERE RESPIRATORY SYNCYTIAL VIRUS INFECTION IN KOREAN INFANTS BORN 32–35 WEEKS' GESTATIONAL AGE

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Why did we perform this research?

- Palivizumab has been available for the prevention of respiratory syncytial virus hospitalisation (RSVH) of high-risk infants in Korea since 2005[1]
- Current Korean guidelines recommend the use of palivizumab in infants born at 32–35 weeks' gestational age (wGA) who are considered at increased risk of RSVH by being born during the RSV season and having a sibling
- An alternative method of identifying 32–35wGA infants at increased risk of RSVH is the International Risk Scoring Tool (IRST), which uses 3 risk factors: 1. Birth 2 months before to 3 months after the RSV season start; 2. Smokers in the household and/or smoking while pregnant; and 3. Siblings/daycare

Objective: To examine the potential impact of utilising the IRST to target prophylaxis against severe RSV infection rather than the current Korean guidelines on the cost-utility of palivizumab (*versus* no intervention) in infants born 32–35wGA

Summary

Previous published cost-utility model of palivizumab in 32-35 wGA infants[2]

International RST[3]
– High + moderate risk groups

versus

Korean Guidelines
– Born within RSV season and presence of sibling(s)

New cost-utility (CU) model

Key data sources
– RSVH rates from IRST[3] (32-35 wGA)
– ICU rates,[4] RSVH and ICU costs,[4,5] and LTRM costs[6] from Korean data
– MARI rates from RCT of PVZ *vs* MVZ[7]
– PVZ efficacy from IMpact trial[8]

Moderate- and high-risk by the IRST ₩26,166,959/QALY

Korean-specific CU model

Korean Guidelines ₩33,268,100/QALY

CU: cost-utility; ICU: intensive care unit; IRST: International Risk Scoring Tool; LTRM: long-term respiratory morbidity; MARI: medically-attended RSV infection not requiring hospitalisation; MVZ: motavizumab; PVZ: palivizumab; RCT: randomised controlled trial; RST: Risk Scoring Tool; RSV: respiratory syncytial virus; RSVH: RSV hospitalisation; QALY: quality-adjusted life year;

Key takeaway

Use of the IRST to selectively target 32–35wGA infants for palivizumab prophylaxis further improves the cost-utility of prophylaxis *versus* current Korean guidelines; consideration should be given to the local application of the IRST

IRST: International Risk Scoring Tool; wGA: weeks' gestational age

What did we find?

Palivizumab prophylaxis of 32–35wGA infants was cost-effective *versus* no intervention from the Korean healthcare perspective when prophylaxis was guided by the IRST or current guidelines (Table 1)

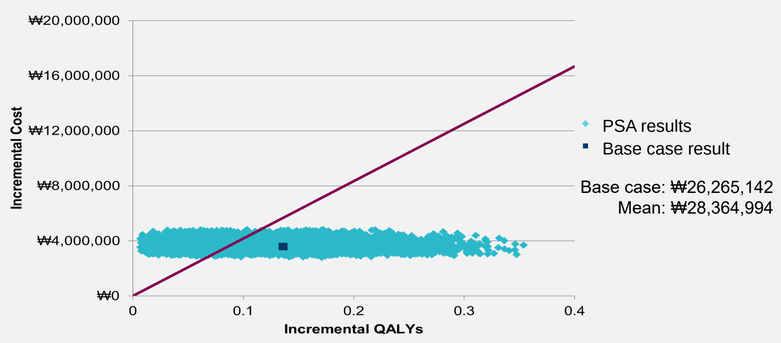
- The cost/quality-adjusted life year (QALY) for prophylaxis of infants scored moderate- and high-risk by the IRST was Korean Won (₩) 26,265,142 *versus* ₩29,516,126 when using birth within season together with siblings (Table 1)
- Probabilistic sensitivity analyses (PSA; 10,000 iterations) resulted in:
  - A 70.8% probability of cost-effectiveness for IRST-guided prophylaxis (Figure 1) against a threshold of ₩41,655,203, the gross domestic product *per* capita of Korea
  - A 67.3% probability for prophylaxis guided by birth within season together with siblings (Figure 2) against a threshold of ₩41,655,203, the gross domestic product *per* capita of Korea
- In deterministic sensitivity analyses the model was most sensitive to long-term morbidity rate, palivizumab efficacy, and palivizumab cost (Figure 3)

Table 1. Risk factor-guided prophylaxis was a cost-effective strategy *versus* no prophylaxis

	32–35 wGA High + moderate risk groups	32–35 wGA Born within RSV season + siblings
Cost difference (₩)	3,573,521	3,610,572
QALY difference	0.136	0.122
ICUR (₩)	**26,265,142**	**29,516,126**

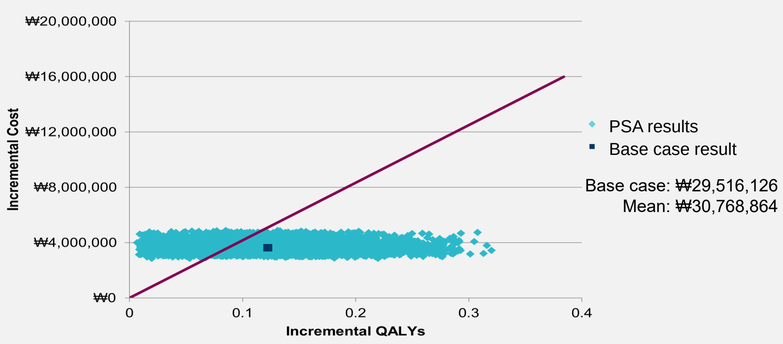
ICUR: incremental cost-utility ratio; QALY: quality-adjusted life year; wGA: weeks' gestational age

Figure 1. PSA demonstrated that the probability of cost-effectiveness for IRST-guided prophylaxis was 70.8% at a willingness-to-pay threshold of ₩41,655,203



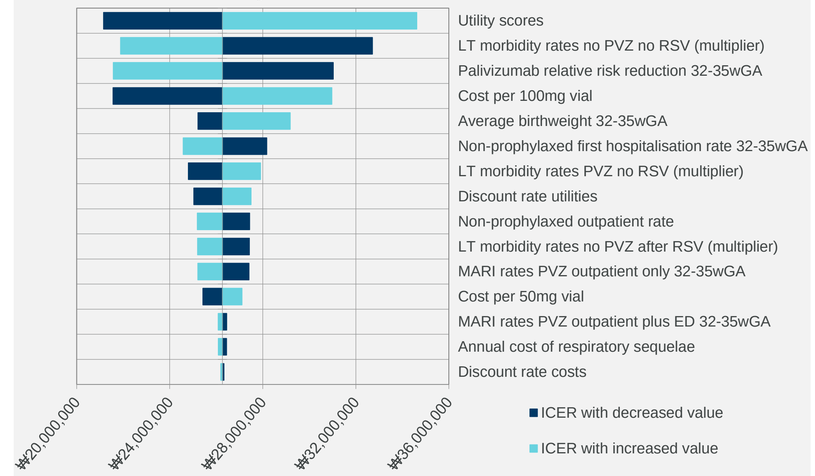
IRST: International Risk Scoring Tool; PSA: Probabilistic sensitivity analysis; QALY: quality-adjusted life year

Figure 2. PSA demonstrated that the probability of cost-effectiveness for Korean guideline- guided prophylaxis was 67.3% at a willingness-to-pay threshold of ₩41,655,203



PSA: Probabilistic sensitivity analysis; QALY: quality-adjusted life year

Figure 3. Deterministic sensitivity analysis (15 most sensitive variables)



Moderate- and high-risk groups for 32-35 wGA, International Risk Scoring Tool, 18-year morbidity with lifetime horizon; ED: emergency department; ICER: incremental cost-effectiveness ratio (cost per quality-adjusted life year expressed in Korean Won); ICU: intensive care unit; LT: long-term; MARI: medically-attended RSV not requiring hospitalisation; PVZ: palivizumab; wGA: weeks' gestational age

Limitations

- Availability of gestational age specific data on resource utilisation and/or costs and long-term respiratory morbidity data beyond age 6 years are lacking as are up to date peri- and post-hospitalisation utilities

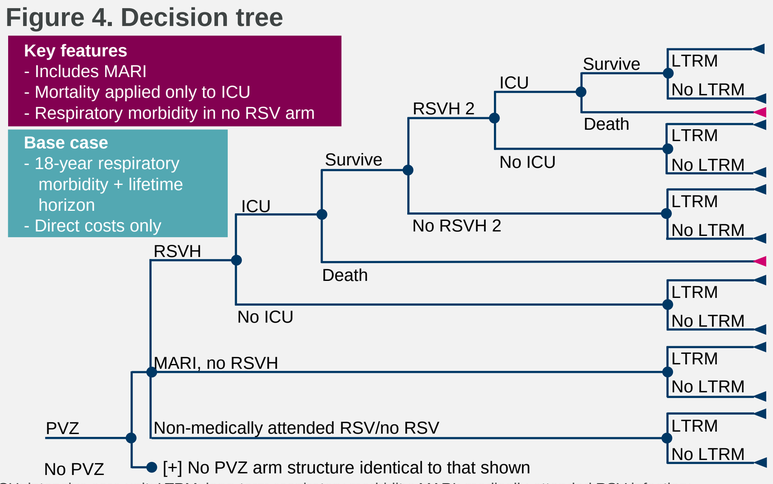
What is the significance of these data?

- **This analysis confirms the cost-utility of palivizumab in preventing RSVH in infants born at 32–35 wGA from the Korean healthcare system perspective**
- **Use of the IRST improves cost-effectiveness *versus* current Korean guidelines**

How did we perform this research?

- Palivizumab prophylaxis was compared to no prophylaxis in 32–35wGA infants either identified as being at moderate- or high-risk of RSV hospitalisation (RSVH) by the IRST[3] (score ≥20/56) or born within the RSV season and having sibling(s) as *per* Korean guidelines
- A previously published cost-utility model was adapted for the Korean setting using, where available, country-specific parameters[2]
- Infants followed a new decision tree based on a systematic review of previous economic evaluations of palivizumab in 32–35wGA infants and input from global and national clinical and health economic experts (Figure 4)
  - Infants experienced RSVH, medically attended RSV infection not requiring hospitalisation (MARI), or were uninfected/non-medically attended
  - Infants admitted to the intensive care unit (ICU) could subsequently suffer mortality; survivors could be readmitted to hospital for RSV infection
  - All surviving infants had the potential to experience long-term respiratory morbidity (LTRM)
- RSVH rates were predicted using the database (N=13,475) that generated the IRST: 6.3% for infants who had high- and moderate-risk scores by the IRST[3] and 4.0% for infants born in season with sibling(s), discounting all other risk factors; palivizumab efficacy at reducing RSVH was 82.2% (IMpact-RSV trial)[8]
- Prophylaxis costs were calculated using Korean palivizumab vial prices,[9] published birthweights[10] and a growth algorithm[11] (Table 3)
  - Mean number of palivizumab doses *per* infant was 4.09
  - No vial sharing was assumed commensurate with the palivizumab Summary of Product Characteristics
- Healthcare costs were drawn from Korean studies where available[3–5,10,12] (Table 3)
- LTRM was assessed up to age 18 years across a lifetime horizon among RSVH, MARI, or uninfected/non-medically attended infants (Table 4)
  - LTRM rates were drawn from the SPRING[13] study up to 6 years of age and from Sigurs *et al.*[14–16] thereafter
  - The impact of palivizumab on LTRM was modelled based on data from three studies[17–19]
- Costs and utilities were discounted at 4.5% in line with the Korean standard
- Deterministic (±20% on main variables) and probabilistic (10,000 iterations) sensitivity analyses were undertaken
- Results were expressed as an incremental cost *per* quality-adjusted life year (QALY; also called incremental cost-utility ratio [ICUR]) *versus* no prophylaxis

Figure 4. Decision tree



ICU: intensive care unit; LTRM: long-term respiratory morbidity; MARI: medically-attended RSV infection; PVZ: palivizumab; RSVH: respiratory syncytial virus hospitalisation

Table 2. Model inputs

Parameter	Palivizumab	No palivizumab
RSVH		
- RSVH rate IRST moderate + high risk[3,8]	1.12%,	6.3%,
- RSVH rate born in season + siblings[3,8]	0.71%	4.0%
- ICU rate[4]	4.2%	4.2%
- Hospital ward length of stay, mean days[4]	5.75	5.75
- Utility in hospital[20,21]	0.60	0.60
- Utility post discharge, no sequelae[22]	0.88	0.88
- Utility post discharge, long-term sequelae[23]	0.79	0.79
- Mortality (ICU patients only)[24,25]	0.43%	0.43%
MARI		
- Rates		
- Outpatient only rate[8,26,27]	2.48%	13.92%
- Outpatient plus ED	0.42%	2.36%
- ED only	0.05%	0.29%
- Utility no sequelae[22]	0.95	0.95
- Utility long-term sequelae[23]	0.79	0.79
No RSVH/MARI		
- Utility no sequelae[22]	0.95	0.95
- Utility long-term sequelae[23]	0.79	0.79
Birth weight (g)[10]	2356.00	2356.00

ICU: intensive care unit; MARI: medically attended RSV infection (not requiring hospitalisation); RSV: respiratory syncytial virus; RSVH: RSV hospitalisation

Table 3. Direct costs

Parameter	Cost (KRW)
Palivizumab	
- 50mg vial[9]	535,851
- 100mg vial[9]	922,664
- Administration (*per* injection)[5]	4,000
Pre-admission healthcare contact[12]	214,570.48
RSVH *per* stay excluding ICU[4,12]	662,835.67
ICU *per* admittance[4]	15,874,170.69
MARI	
- Outpatient only[12]	71,523.49
- Outpatient plus ED[12]	286,093.97
- ED only[12]	214,570.48
- Follow-up appointment[12]	71,523.49
Respiratory morbidity *per* annum[6]	181,566.60

ED: Emergency Department; ICU: intensive care unit; MARI: medically attended RSV infection (not requiring hospitalisation); RSV: respiratory syncytial virus; RSVH: RSV hospitalisation

Table 4. Long-term respiratory morbidity rates[13–19]

Years	Palivizumab		No palivizumab	
	RSVH	No RSVH	RSVH	No RSVH
0–1	18.43%	5.38%	41.43%	12.09%
1–2	18.43%	5.38%	41.43%	12.09%
2–3	11.05%	5.80%	29.27%	15.36%
3–4	6.12%	4.15%	18.55%	12.57%
4–5	4.39%	2.73%	15.00%	9.31%
5–6	3.25%	2.53%	12.39%	9.66%
6–7	2.93%	2.29%	12.39%	9.66%
7–13	2.33%	1.47%	17.39%	10.96%
13–18	1.79%	1.17%	22.39%	14.66%

RSVH: respiratory syncytial virus hospitalisation

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- BRG, IK & JF employers have received payment from AstraZeneca for work on various projects
- JMK, HYJ &YSC & JET declare no conflict of interest

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