



# MenACWY-TT Aşısı (Nimenrix®-Pfizer)

Feyza Koç



# Sunum akışı

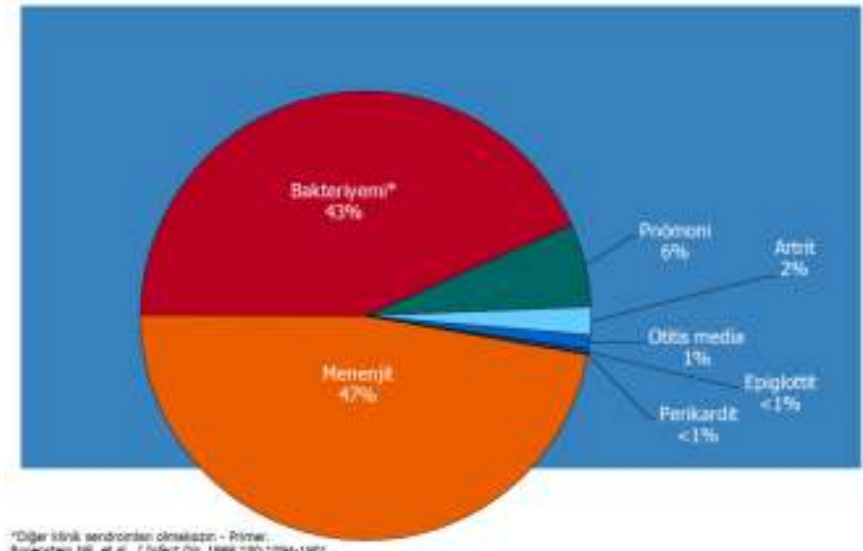
- Meningokok enfeksiyonlarından korunmak için aşı gerekli mi?
- Hangi aşı tercih edilmelidir? (polisakkarit-konjuge)
- Türkiye'de bulunan konjuge aşılar
- MenACWY-TT (Nimenrix®) aşısının özellikleri
  - 1) Aşının içeriği
  - 2) Türkiye'deki serogrupları kapsıyor mu?
  - 3) Hangi yaş ve kaç doz?
  - 4) Aşının koruyuculuğu
  - 5) Aşının koruyuculuk süresi
  - 6) Yan etkileri
  - 7) Diğer aşılarla uygulanması

**Meningokok enfeksiyonlarından  
korunmak için aşı gerekli mi?**

# Meningokok enfeksiyonları

Dünyada ve Türkiye'de menenjitin en sık nedeni: Meningokok

- Her yıl 1.200.000 olgu → 135.000 ölüm
- Menenjitte ölüm hızı → %5-10
- Sepsiste ölüm hızı → %15-20



# Meningokok enfeksiyonları için risk faktörleri

Yaş	Nazofaringeal irritasyon	Sosyal faktörler	Konağa ait
✓İnfant ✓Ergen	✓Sigara ✓Solunum yolu enfeksiyonları	✓Sağlık çalışanları ✓Toplu yaşam (öğrenci,asker) ✓Endemik bölgeye seyahat (Hac) ✓Aşırı alkol tüketimi	✓Oponizasyon ve fagositoz bzk ✓Properdin eksikliği ✓C5-C9 kompleman yolunda defekt ✓Nefrotik sendrom ✓Hipogamaglobulinemi ✓Splenektomi veya fonk aspleni ✓HIV ✓Genetik polimorfizm (MBL, TLR4 gen.....)

## ABD'de

- 159 çocuk → 9 (%5,6)'unda altta yatan hastalık
- 9 çocuk → 2'si kompleman eksik

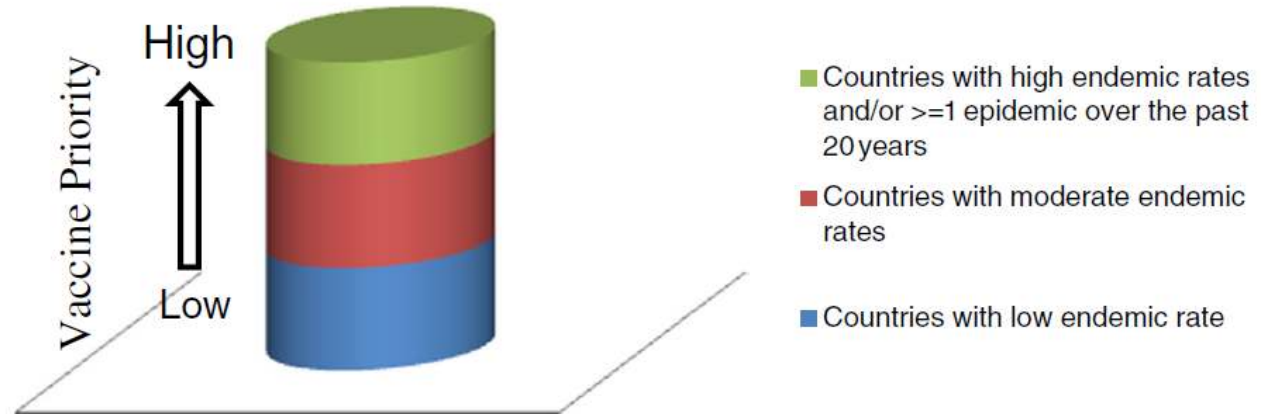
## İspanya'da

- 1255 çocuk → 46 (%3.5)'sında altta yatan hastalık

**Meningokok hastalıklarının çoğu daha önce tanımlanmış bir risk faktörü olmayan sağlıklı bireylerde görülür**

lece  
man

**Meningokokal hastalıklar DSÖ tarafından aşı ile engellenebilir hastalık nedeni olarak tanımlanmıştır**



# Türkiye'de....

**Table 2 Countries with moderate endemic rates (2–10 cases/100,000 population per year)**

Country	Year	Incidence/ 100,000 population	Predominant serogroup	Source	Comments
Switzerland	1999–2004	1.16–2.36	C	[24]	A conjugate vaccine for group C introduced in 2005
Turkey	1997–2005	0.3–2.2	*	[28]	
United Kingdom	1999–2010	5.4 (pre-vaccine) 1.63 (post vaccine)	B, C	[23,24]	A conjugate vaccine for group C introduced in 1999

**Yüksek endemi: 100.000 de  $\geq$  10 olgu**

**Orta endemi: 100.000 de 2-10 olgu**

**Düşük endemi: 100 000 de  $<$  2 olgu**



# Türkiye'de.....

**2005 – 2006 yıllarında yapılan çalışmada**

Meningokoksik menenjit 1,99/100.000

**2006-2012 yıllarında yapılan çalışmada**

İnvaziv meningokok enfeksiyonu 100.000'de 4

Menenjitte ölüm hızı %3.3 (%55'i meningokoksik menenjit)

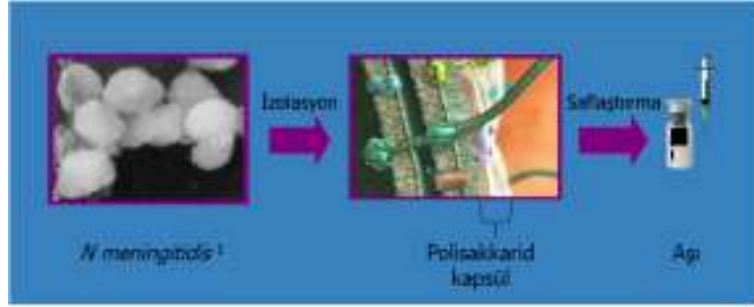
Ceyhan M, et al. *Emerging Infectious Diseases*. 2008;14 (7):1089-96.

Ceyhan M, Gürler N, Ozsurekci Y et al. *Meningitis caused by neisseria meningitidis, hemophilus influenzae type B and streptococcus pneumoniae during 2005-2012 in Turkey. A multicenter prospective surveillance study. Hum Vaccin Immunother* 2014;10(9): 2706–2712.

**Hangi aşı tercih edilmelidir**

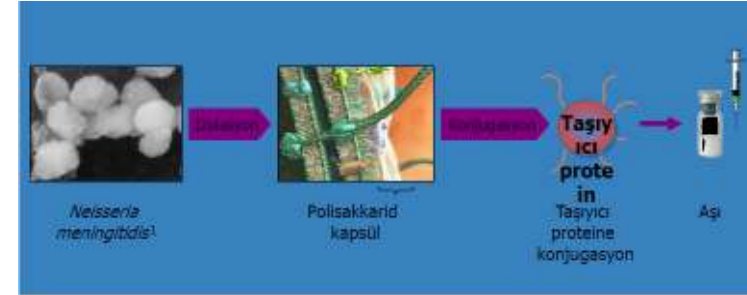
Polisakkarit aşı-Konjuge aşı

## Polisakkarit aşılar



- T-hücre bağımsız yanıt, B lenfositleri uyarırlar, <2 yaş yeterli bağışık yanıt Ø
- Aşının koruyuculuğunun devamı için tekrarlamak gerekli
- Asemptomatik taşıyıcılığı önlemezler

## Konjuge aşılar



- Meningokok polisakkaridlerinin ya da oligosakkaridlerinin çeşitli proteinlerle konjuge edilmesi
- T hücre aracılıklı yanıtı uyararak < 2 yaş çocuklarda bağışık yanıtın oluşmasını sağlamaktadır
- Aşının koruyuculuk süresi daha uzundur
- Asemptomatik taşıyıcılığı azaltırlar
- Lokal yan etkileri daha sık

Polisakkarit aşılar yerine konjuge aşılar tercih edilmektedir.

# **Türkiye'de bulunan konjuge aşılar**

- 1) **MenACWY-TT konjuge aşısı (Nimenrix<sup>®</sup>-Pfizer)**
- 2) **MenACWY-DT konjuge aşısı (Menactra<sup>®</sup>-Sanofi Pasteur)**
- 3) **MenACWY-CRM konjuge aşısı (Menveo<sup>®</sup>-GSK)**

# **MenACWY-TT Aşısının özellikleri**

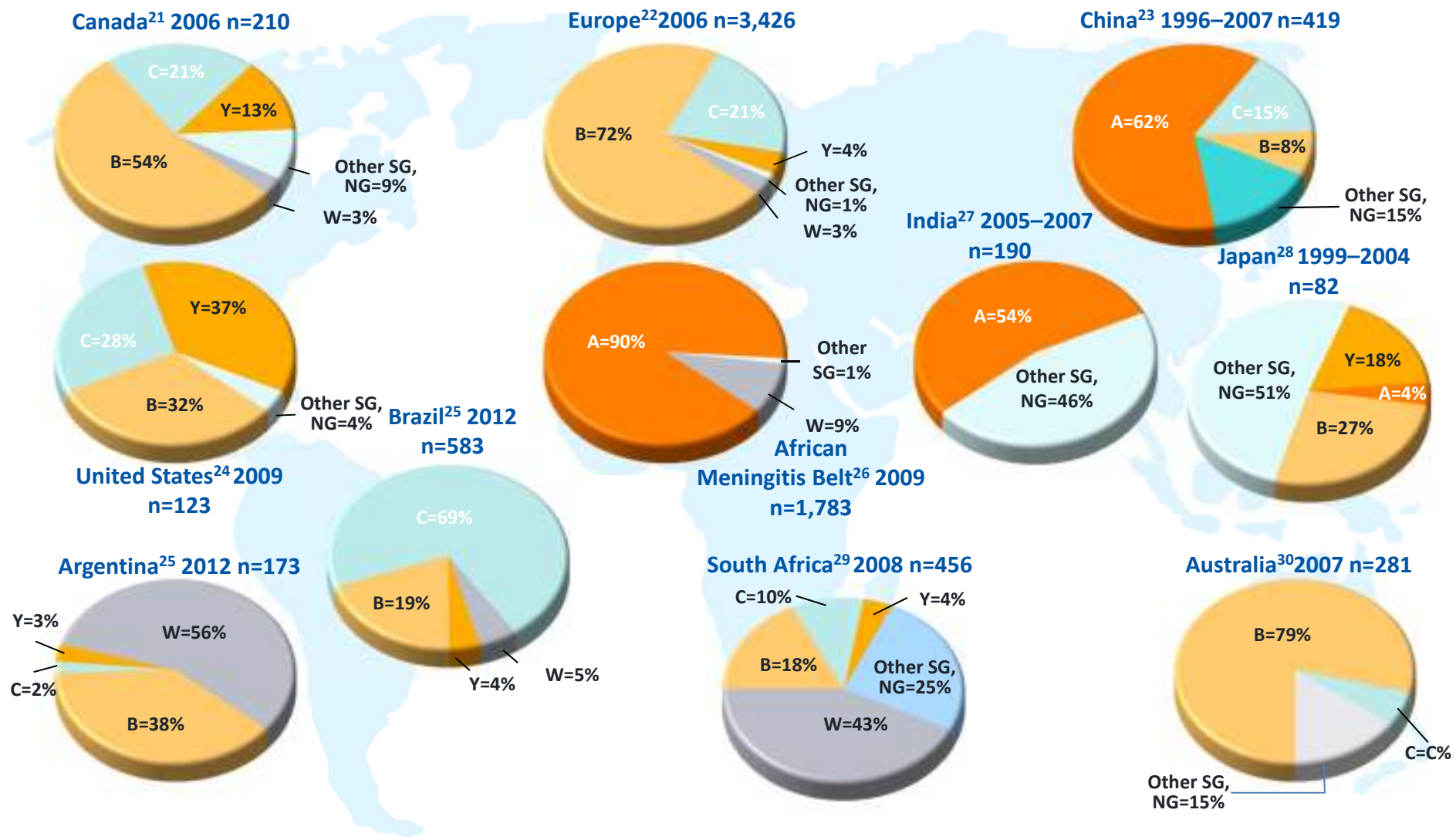
# Aşının içeriği

- Nisan 2013'de Avrupa'da kullanılmaya başlanmıştır
- Türkiye'de Temmuz 2013'ten beri ruhsatlı
- Serogrup A,C,W,Y kapsül polisakkaritleri (5 µg)
- Taşıyıcı protein tetanoz toksoidi (TT) (44 µg)
- Yardımcı madde sukroz, trometamol, sodyum klorür
- Adjuvan ve thimerosal içermez
- 0,5 ml, IM

**Türkiye'deki serogrupları kapsıyor mu?**

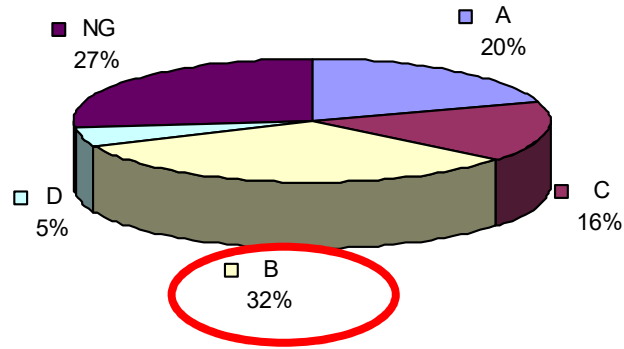


# Dünyada serogrup dağılımı

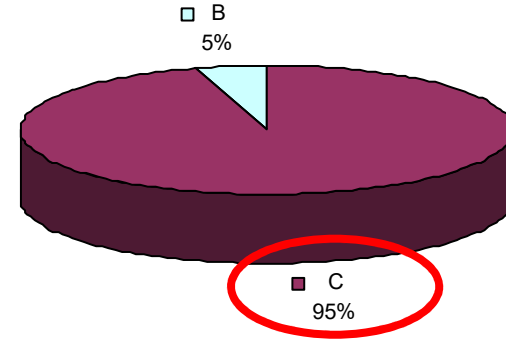


# Türkiye’de Serogrup Dağılımı

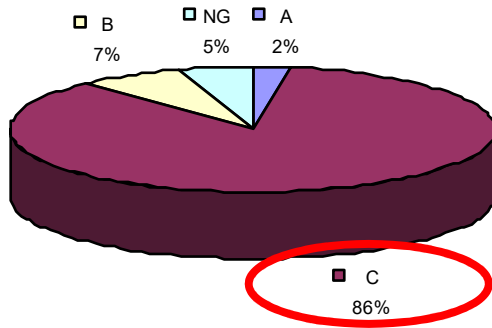
Berkman, 1974-1981, Ankara, n:205



Tuncer, Ocak –Haziran 1987, Sami Ulus, n:41



Elmastaş, 1990-1991, Behçet Uz, n:41



Ceyhan, 2005-2006, Çok merkezli, n:138

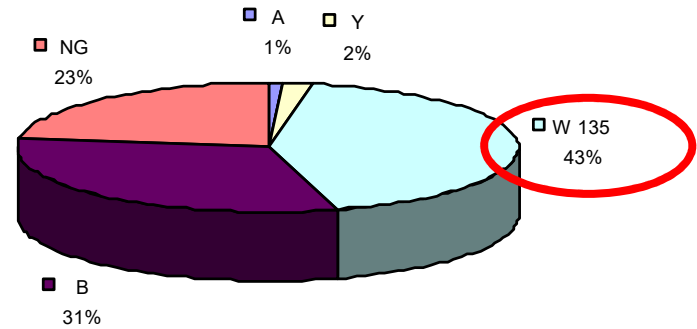


Table 1. Distribution of causative agents of bacterial meningitis and meningococcal serogroups per year in Turkey

Study Period (Year)	2005-2006		2007-2008		2009-2010		2011-2012		2005-2012	
	n	%	n	%	n	%	n	%	n	%
Serogroup W-135	59	42.7	19	17.6	23	56.1	26	56.5	127	38.1
Serogroup B	43	31.1	38	35.1	3	7.3	3	6.5	87	26.1
Serogroup A	1	0.8	9	8.3	15	36.6	3	6.5	28	8.4
Serogroup C	0	0	0	0	0	0	0	0	0	0
Serogroup Y	3	2.2	0	0	0	0	0	0	3	0.9
Nongroupable	32	23.2	42	39	0	0	14	30.5	88	26.4

Çok merkezli, 1-18 yaş, 1452 çocuk, 645'i  
PCR ile menenjit tanısı

## Türkiye 2013-2014...

Table 1. Distribution of causative agents of bacterial meningitis and meningococcal serogroups during 2013–2014 in Turkey.

Study Period (Year) Causative Bacteria	2013		2014		2013–2014 (2 years)	
	n	%	n	%	n	%
Serogroup W-135	7	36.8	29	43.9	36	42.4
Serogroup B	5	26.4	23	34.9	28	32.9
Serogroup A	0	0	3	4.5	3	3.5
Serogroup C	0	0	0	0	0	0
Serogroup Y	0	0	2	3.0	2	2.4
Nongroupable	7	36.8	9	13.7	16	18.8
<i>N. meningitidis</i> (Total)	19	86.4	66	91.7	85	90.4
<i>S. pneumonia</i>	3	13.6	6	8.3	9	9.6
<i>H. influenzae</i> type b	0	0	0	0	0	0
Total number of Positive Samples	22	100	72	100	94	100

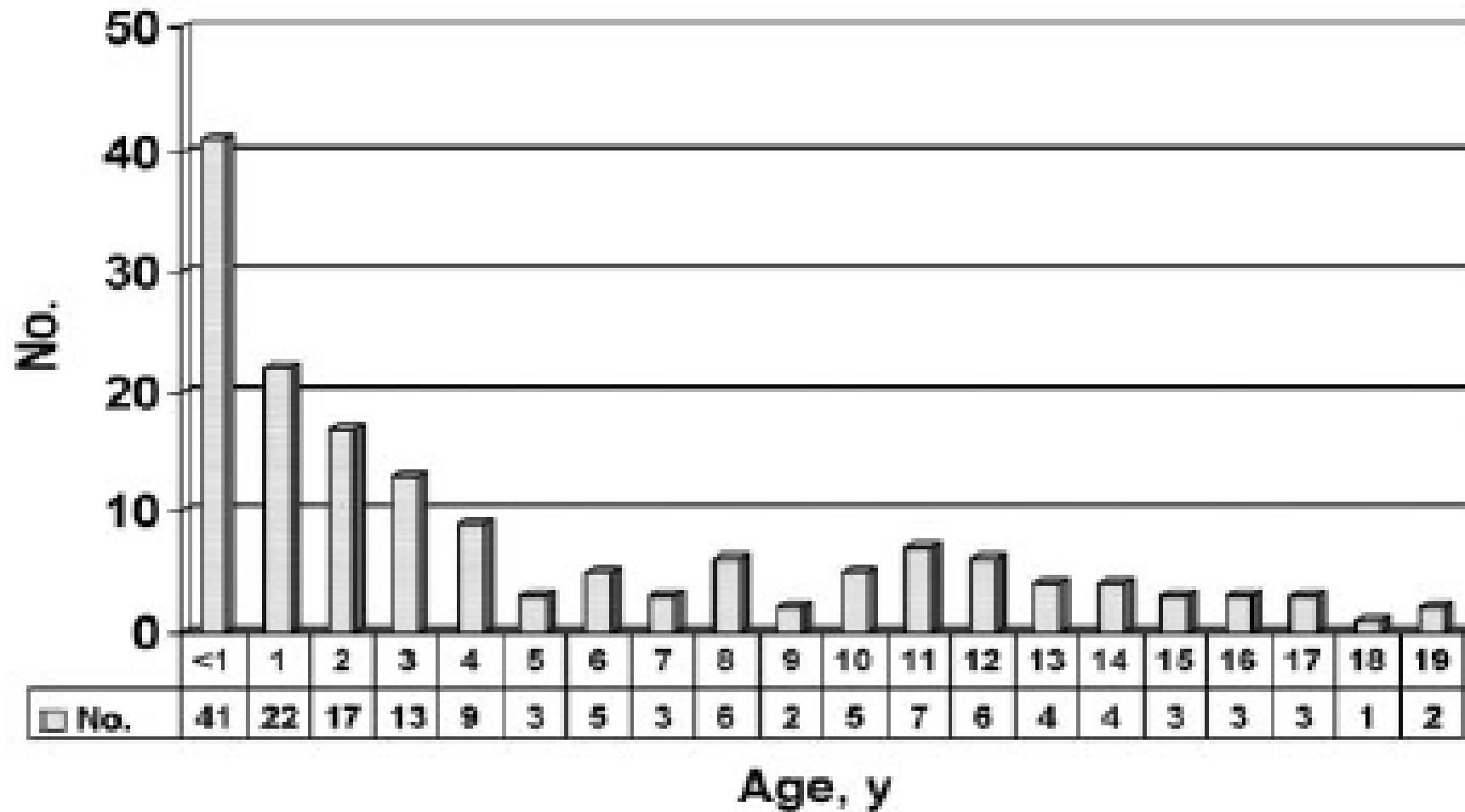
# Taşıyıcılık??

- 10-24 yaş arası 1500 olgu
- *Neisseria meningitidis* taşıyıcılığı %6.3 (n=96)
- Serogup:
  - 63 serogrup W (%65.6)
  - 5 serogrup A (%5.2)
  - 4 serogrup Y (%4.1)
  - 9 serogrup B (%9.3)
  - 14 gruptandırılmayan
  - Hiçbir örnekte serogrup C saptanmadı.

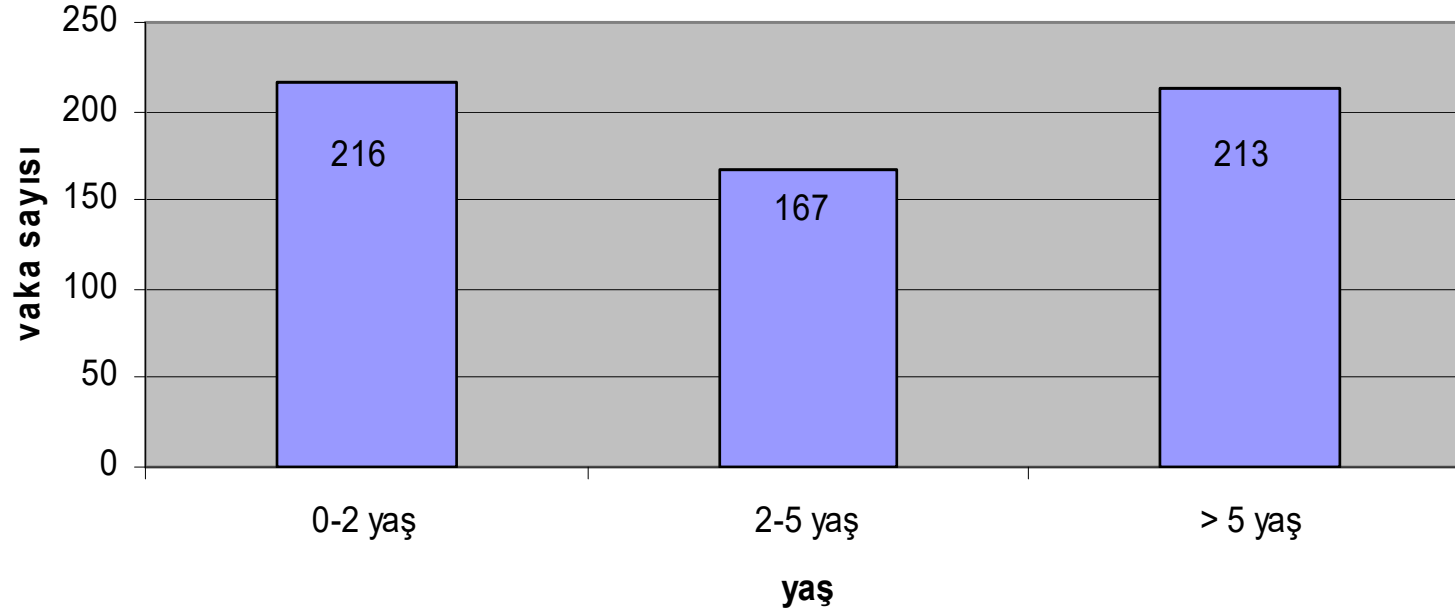
# Aşı hangi yaş grubuna ve kaç dozda yapılıyor?

- 12 ay üzerinde kullanılabilir
- Tek doz olarak uygulanır

## Farklı ülkeler farklı yaş grupları....



# Olguların yaş grubuna göre dağılımı

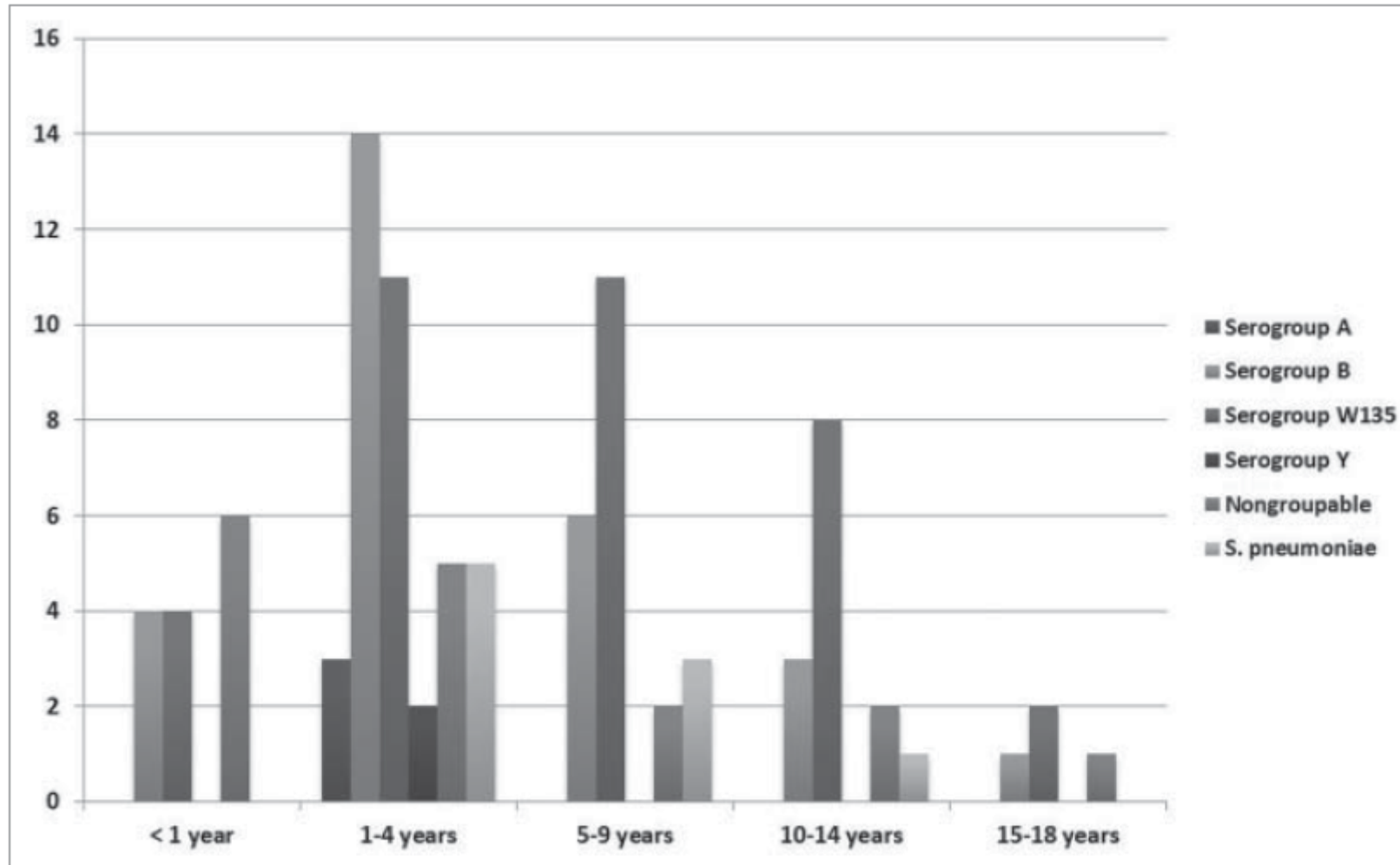


n:596, 0-15 yaş

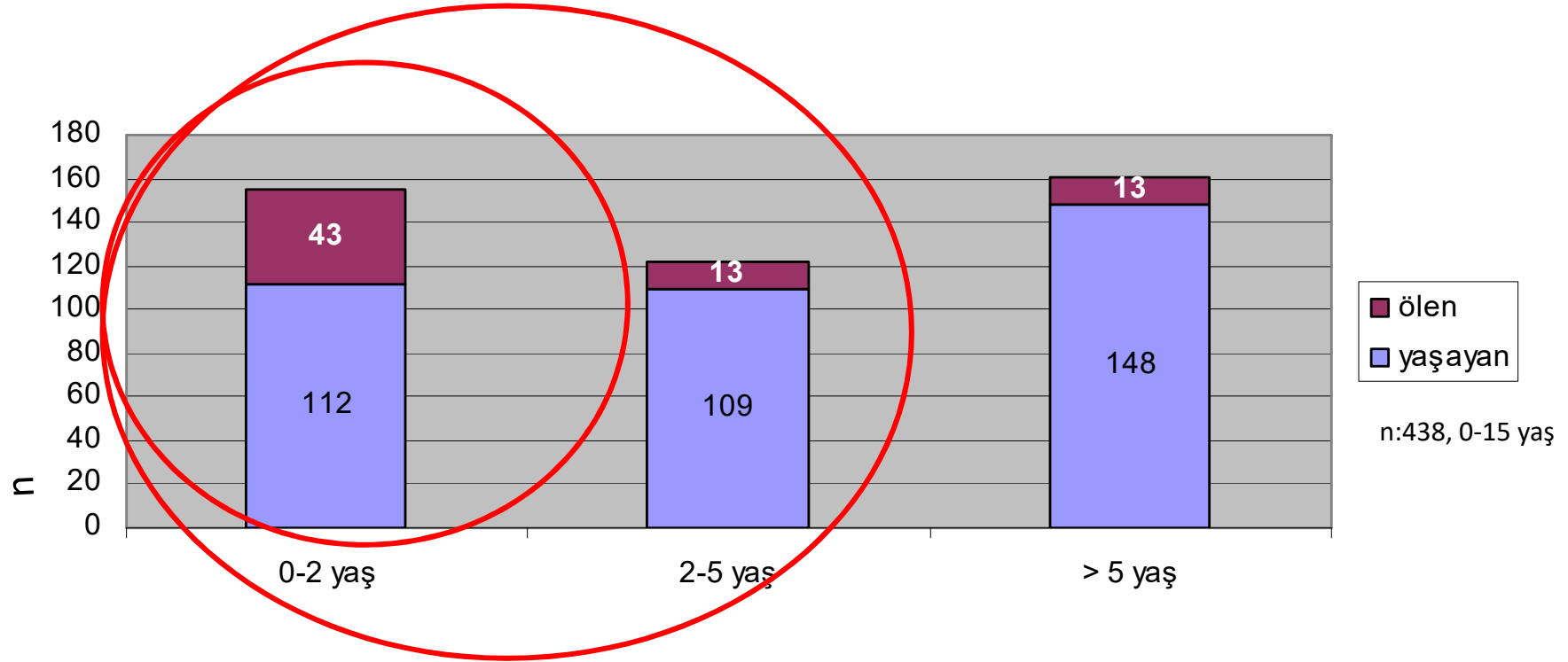
Adölesan piki 2005 yılından sonraki çalışmalarda gözlenmedi.



# Türkiye’de hastalar....



# Türkiye'de Hasta ve Ölümler



**Ölümlerin % 70,9 'u 5 yaş altında**

**Ölümlerin % 62,3'ü 2 yaş altında**

# **Aşının koruyuculuğu ve antikor yanıtları**

# MenACWY-TT'nin Faz II-III Klinik Çalışmaları

**Table 4** Phase II and Phase III clinical vaccination trials of MenACWY-TT conjugate vaccine in infants, toddlers, and children

Phase	Author	Year	Age group	Country	Registry number at Clinicaltrials.gov
II	Klein et al <sup>89</sup>	2013	9–12 months	United States	NCT00471081
II	Vesikari et al <sup>90</sup>	2012	12–23 months	Finland	NCT00427908
II	Knuf et al <sup>87</sup>	2010	2–10 years	Finland	
II	Knuf et al <sup>87</sup>	2010	12–14 months	Germany	NCT00126984
II	Knuf et al <sup>88</sup>	2012	3–5 years	Austria	
II	Knuf et al <sup>88</sup>	2012	12–14 months	Germany	NCT00126984
II	Knuf et al <sup>88</sup>	2012	3–5 years	Austria	
II	Dbaiibo et al <sup>94</sup>	2012	4.5–10 years	Lebanon	NCT00661557
III	Ruiz-Palacios et al <sup>105</sup>	2013	12–23 months	Taiwan	NCT00758264
III	Ruiz-Palacios et al <sup>105</sup>	2013	12–23 months	Mexico	
III	Vesikari et al <sup>91</sup>	2011	12–23 months	Finland	NCT00474266
III	Knuf et al <sup>106</sup>	2011	12–23 months	Austria	NCT00508261
III	Knuf et al <sup>106</sup>	2011	12–23 months	Germany	
III	Knuf et al <sup>106</sup>	2011	12–23 months	Greece	
III	Memish et al <sup>93</sup>	2011	2–10 years	Philippines	NCT00514904
III	Memish et al <sup>93</sup>	2011	2–10 years	India	
III	Memish et al <sup>93</sup>	2011	2–10 years	Lebanon	
III	Memish et al <sup>93</sup>	2011	2–10 years	Saudi Arabia	
III	Knuf et al <sup>95</sup>	2013	2–10 years	Germany	NCT00674583
III	Knuf et al <sup>95</sup>	2013	2–10 years	France	

**Abbreviation:** MenACWY-TT, serogroups A, C, W-135, and Y tetanus toxoid conjugate vaccine.

# MenACWY-TT'nin Faz II-III Klinik Çalışmaları

**Table 5** Phase II and phase III clinical vaccination trials of MenACWY-TT conjugate vaccine in adolescents and adults

Phase	Author	Year	Age group	Country	Registry number at Clinicaltrials.gov
II	Dbaiibo et al <sup>94</sup>	2012	11–34 years	Lebanon	NCT00661557
II	Ostergaard et al <sup>99</sup>	2013	15–19 years	Denmark	NCT00390143
II	Baxter et al <sup>100</sup>	2011	10–25 years	USA	NCT00454909
II	Ostergaard et al <sup>96</sup>	2009	15–19 years	Belgium	NCT00126945
			18–25 years	Denmark	NCT00196950
II	Borja-Tabora et al <sup>98</sup>	2013	11–55 years	Philippines	NCT00356369
				Saudi Arabia	
III	Ostergaard et al <sup>103</sup>	2012	11–17 years	Sweden	NCT00465816
				Denmark	
III	Bernal et al <sup>97</sup>	2011	11–17 years	Philippines	NCT00464815
				India	
				Taiwan	
III	Dbaiibo et al <sup>85</sup>	2012	18–55 years	Lebanon	NCT00453986
				Philippines	
III	Aplasca-De Los Reyes et al <sup>104</sup>	2012	18–55 years	Lebanon	NCT00453986
				Philippines	
III	Dbaiibo et al <sup>46</sup>	2013	56–103 years	Lebanon	NCT01235975

**Abbreviation:** MenACWY-TT, serogroups A, C, W-135, and Y tetanus toxoid conjugate vaccine.

# Konjuge meningokok aşıları koruma göstergeleri

İnsan komplemanı serum bakterisidal antikor (hSBA) analizleri

≥1:4 değerindeki hSBA titreleri, koruma eşik değeri olarak kabul edilir

Tavşan komplemanı serum bakterisidal antikor (rSBA) analizleri

≥1:8 değerindeki rSBA titreleri, koruma eşik değeri olarak kabul edilir.

**GMT : Geometrik Ortalama Titre**  
Serumda bulunan antikor titrelerini gösterir

**İnsan veya yavru tavşan komplemanı kullanılan SBA analizleri, DSÖ<sup>3</sup> ve ruhsatlandırma kurumları tarafından kabul edilmektedir<sup>4</sup>**

# ilk 2 yaşta

Vaccine 28 (2010) 744–753



Contents lists available at ScienceDirect

Vaccine

journal homepage: [www.elsevier.com/locate/vaccine](http://www.elsevier.com/locate/vaccine)



A dose-range study assessing immunogenicity and safety of one dose of a new candidate meningococcal serogroups A, C, W-135, Y tetanus toxoid conjugate (MenACWY-TT) vaccine administered in the second year of life and in young children

M. Knuf<sup>a</sup>, D. Kieninger-Baum<sup>a</sup>, P. Habermehl<sup>a</sup>, P. Muttonen<sup>b</sup>, H. Maurer<sup>c</sup>, P. Vink<sup>d</sup>, J. Poolman<sup>d</sup>, D. Boutriau<sup>d,\*</sup>

# 12-23 ay arası çocuklarda

## A B S T R A C T

Tetavalent meningococcal serogroups ACWY conjugate vaccines will provide an advantage to those at most risk of invasive meningococcal disease; namely young children. Co-administration of ACWY-TT with DTaP-HBV-IPV/Hib was assessed in a randomized trial in 793 children aged 12–23 months. Pre-specified criteria for non-inferiority of immunogenicity following co-administration versus separate ACWY-TT and DTaP-HBV-IPV/Hib administration were reached. One month post-vaccination,  $\geq 97.3\%$  of ACWY-TT vaccinees had rSBA titres  $\geq 1:8$  (all serogroups). Seroprotection/seropositivity rates against DTaP-HBV-IPV/Hib antigens were  $\geq 98.2\%$ . The safety profile of co-administration was similar to that of DTaP-HBV-IPV/Hib alone. ACWY-TT and DTaP-HBV-IPV/Hib co-administration during the second year would facilitate introduction of ACWY-TT into routine toddler vaccination schedules.

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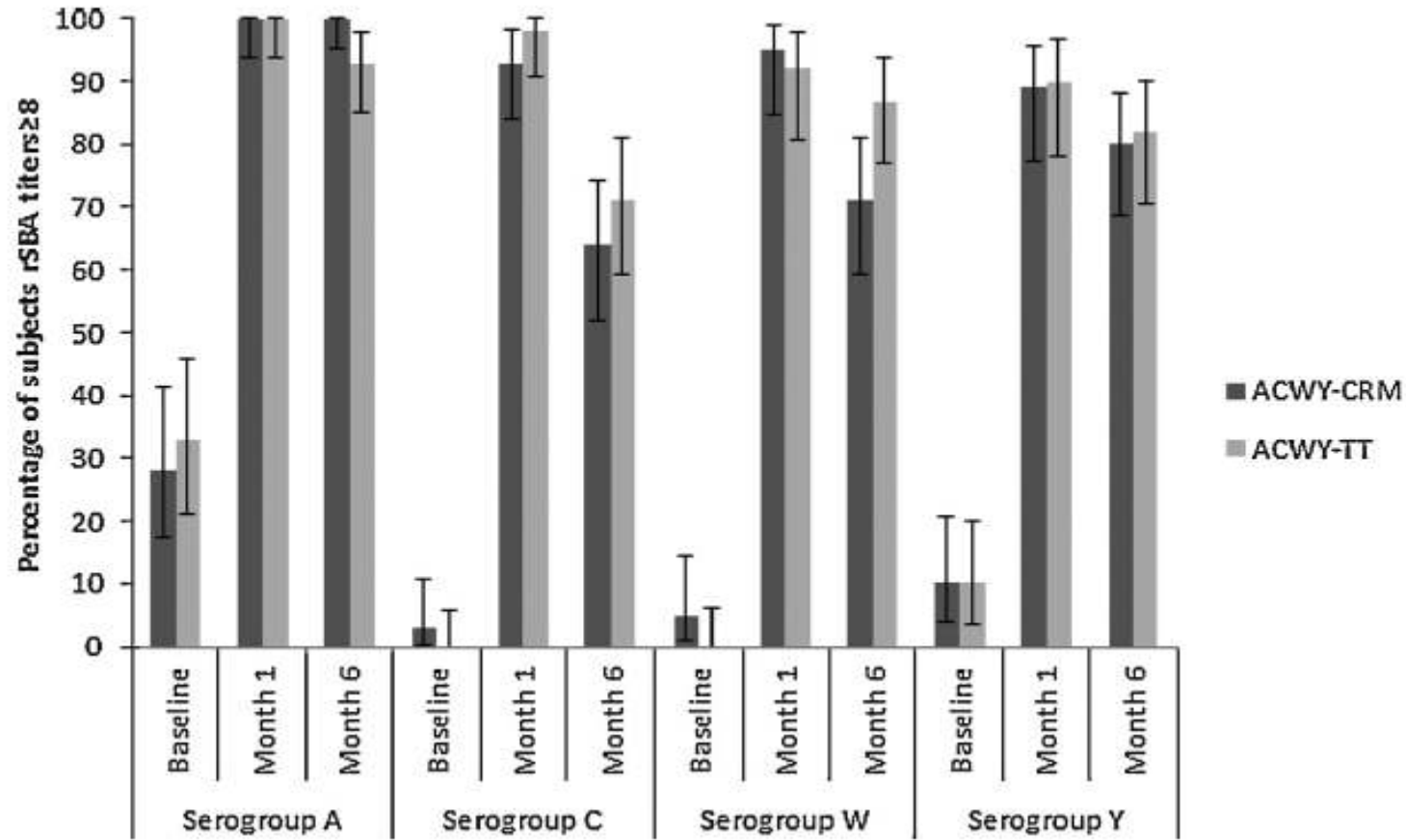
Irmingard Tichmann-Schumann<sup>c</sup>, Hartwig Maurer<sup>a</sup>, Lothar Maurer<sup>b</sup>, Thomas Fischbach<sup>d</sup>,  
Henrike Zinke<sup>i</sup>, Heidemarie Pankow-Culot<sup>j</sup>, Vassiliki Papaevangelou<sup>k</sup>, Veronique Bianco<sup>l</sup>,  
Marie Van der Wielen<sup>l</sup>, Jacqueline M. Miller<sup>m</sup>

**Aşılardan bir ay sonra tüm seroguplara karşı koruyuculuk % 97,3**



# 12-15 ay çocuklarda....

G. Bona et al. / Vaccine 34 (2016) 3363–3370



# 2-10 yaş çocuklarda

Eur J Pediatr (2013) 172:601–612

DOI 10.1007/s00431-012-1924-0

ORIGINAL ARTICLE

## Immunogenicity and safety of the quadrivalent meningococcal serogroups A, C, W-135 and Y tetanus toxoid conjugate vaccine (MenACWY-TT) in 2–10-year-old children: results of an open, randomised, controlled study

Markus Knuf · Olivier Romain · Klaus Kindler ·

Uta Walther · Ph<sup>o</sup> My Tran · Heidemarie Pankow · Culot ·

Thomas Fischbacher ·

Véronique Bianco

Antibody	ACWY-TT	
	<i>N</i>	%
rSBA-MenA	226	94.7
rSBA-MenC	268	94.8
rSBA-MenW-135	282	98.6
rSBA-MenY	285	96.5

# 11-55 yaş ergen ve erişkinlerde

Borja-Tabora *et al. BMC Infectious Diseases* 2013, **13**:116  
<http://www.biomedcentral.com/1471-2334/13/116>



## RESEARCH ARTICLE

## Open Access

**Table 2 Differences in rSBA vaccine response rate between the ACWY-TT and the Men-PS groups**

Antibody	ACWY-TT		Men-PS		Difference in vaccine response rate (ACWY-TT minus Men-PS) % [95% CI]
	N	%	N	%	
rSBA-MenA	289	82.7	99	69.7	13.00 [3.52, 23.50]
rSBA-MenC	324	94.4	113	90.3	4.18 [-1.03, 11.36]
rSBA-MenW-135	326	96.3	109	91.7	4.58 [-0.07, 11.49]
rSBA-MenY	329	93.0	113	85.0	8.05 [1.72, 16.17]

ACWY-TT = group of participants who received one dose of MenACWY-TT at Month 0.

Men-PS = group of participants who received one dose of the MenACWY polysaccharide vaccine at Month 0.

Vaccine response defined as:

- rSBA titre  $\geq 32$  at Month 1 for initially seronegative participants (rSBA titre  $< 8$ ).
- rSBA titre at Month 1  $\geq 4$ -fold the antibody titre at Month 0 for initially seropositive participants (rSBA titre  $\geq 8$ ).

Charissa Borja-Tabora<sup>1</sup>, Cecilia Montalban<sup>2</sup>, Ziad A Memish<sup>3\*</sup>, Marie Van der Wielen<sup>4</sup>, Veronique Bianco<sup>4</sup>, Dominique Boutriau<sup>4</sup> and Jacqueline Miller<sup>5</sup>

## **56-103 yaş yetişkinlerde**

Drugs Aging (2013) 30:309–319  
DOI 10.1007/s40266-013-0065-0

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ORIGINAL RESEARCH ARTICLE

### **Immunogenicity and Safety of a Quadrivalent Meningococcal Serogroups A, C, W-135 and Y Tetanus Toxoid Conjugate Vaccine (MenACWY-TT) Administered to Adults Aged 56 Years and Older: Results of an Open-Label, Randomized, Controlled Trial**

Ghassan Dbaibo · Nabil El-Ayoubi ·  
Soha Ghanem · Farah Hajar · Veronique Bianco ·  
Jacqueline M. Miller · Narcisa Mesaros

**Table 3** Percentage of subjects with rSBA titers  $\geq 1:8$  and  $\geq 1:128$  and GMTs (ATP cohort for immunogenicity)

Serogroup	Group	Time point	N	$\geq 1:8$		$\geq 1:128$		GMT [95 % CI]
				n	% [95 % CI]	n	% [95 % CI]	
A	MenACWY-TT	Pre	181	136	75.1 [68.2; 81.3]	104	57.5 [49.9; 64.8]	108.3 [77.9; 150.5]
		Post	186	185	99.5 [97.0; 100]	177	95.2 [91.0; 97.8]	1,442.3* [1,174.4; 1,771.3]
	MenPS	Pre	61	43	70.5 [57.4; 81.5]	37	60.7 [47.3; 72.9]	102.1 [55.2; 188.7]
		Post	65	65	100 [94.5; 100]	63	96.9 [89.3; 99.6]	2,840.1 [2,062.3; 3,911.1]
C	MenACWY-TT	Pre	190	135	71.1 [64.0; 77.4]	86	45.3 [38.0; 52.6]	71.5 [51.1; 100.1]
		Post	192	192	100 [98.1; 100]	179	93.2 [88.7; 96.3]	2,498.6* [1,887.0; 3,308.2]
	MenPS	Pre	66	44	66.7 [54.0; 77.8]	29	43.9 [31.7; 56.7]	73.8 [38.0; 143.6]
		Post	66	65	98.5 [91.8; 100]	62	93.9 [85.2; 98.3]	4,815.1 [2,827.0; 8,201.2]
W-135	MenACWY-TT	Pre	188	135	71.8 [64.8; 78.1]	98	52.1 [44.7; 59.5]	84.7 [61.1; 117.3]
		Post	193	188	97.4 [94.1; 99.2]	183	94.8 [90.7; 97.5]	1,454.0 [1,130.5; 1,870.1]
	MenPS	Pre	62	40	64.5 [51.3; 76.3]	30	48.4 [35.5; 61.4]	68.5 [37.4; 125.3]
		Post	66	63	95.5 [87.3; 99.1]	62	93.9 [85.2; 98.3]	1,838.4 [1,134.6; 2,978.9]
Y	MenACWY-TT	Pre	189	148	78.3 [71.7; 84.0]	118	62.4 [55.1; 69.4]	137.6 [100.7; 187.9]
		Post	193	193	100 [98.1; 100]	187	96.9 [93.4; 98.9]	2,547.0 [2,059.6; 3,149.8]
	MenPS	Pre	64	55	85.9 [75.0; 93.4]	46	71.9 [59.2; 82.4]	217.4 [131.7; 358.9]
		Post	66	66	100 [94.6; 100]	65	98.5 [91.8; 100]	3,931.6 [2,726.1; 5,670.2]

**Koruyuculuk süresi ve antikor  
yanıtının devamı**

# 12-24 ay bebeklerde 3 yıllık takip sonuçları

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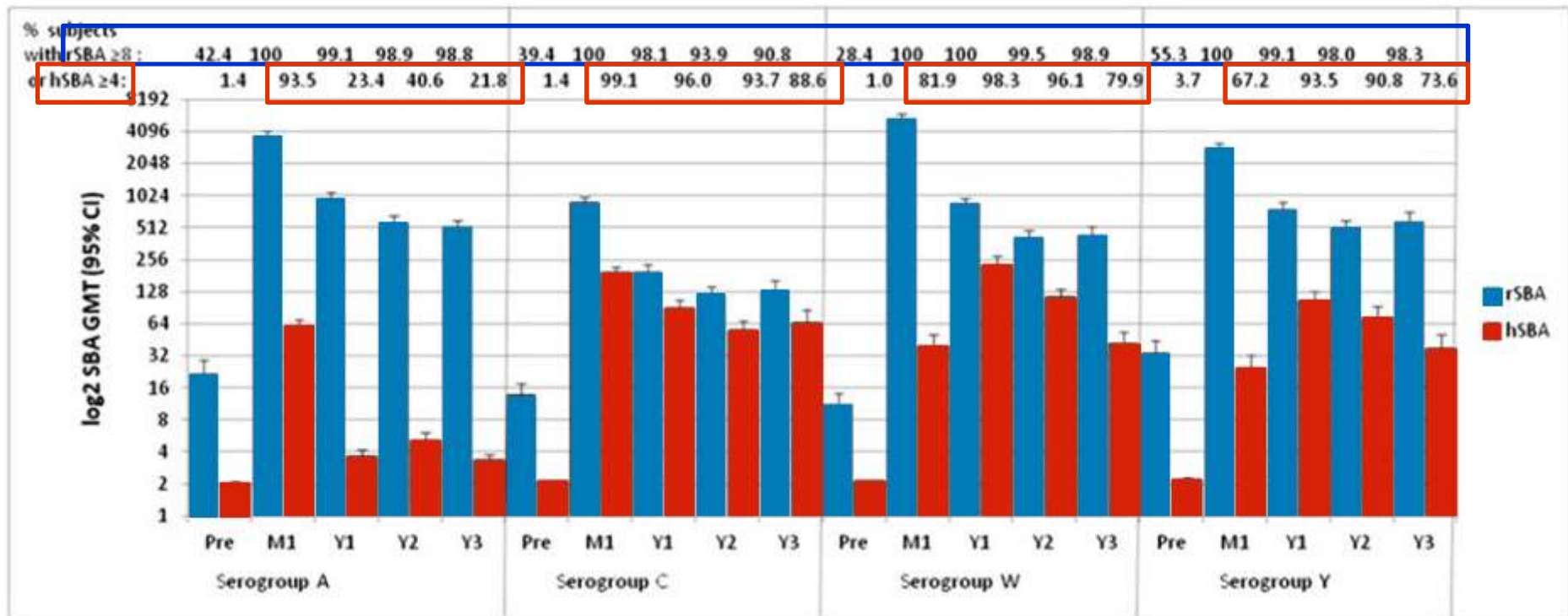
Human Vaccines & Immunotherapeutics 8:12, 1892–1903; December 2012; © 2012 Landes Bioscience

**Randomized trial to assess the immunogenicity, safety and antibody persistence up to three years after a single dose of a tetravalent meningococcal serogroups A, C, W-135 and Y tetanus toxoid conjugate vaccine in toddlers**

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Timo Vesikari,<sup>1,\*</sup> Aino Forstén,<sup>1</sup> Dominique Boutriau,<sup>2</sup> Véronique Bianco,<sup>2</sup> Marie Van der Wielen<sup>2</sup> and Jacqueline M. Miller<sup>3</sup>

# Antikor yanıtının devamı





# 2-10 yaş çocuklarda 3 yıllık takip sonuçları

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Human Vaccines & Immunotherapeutics 8:12, 1882–1891; December 2012; © 2012 Landes Bioscience

**A randomized study to assess the immunogenicity, antibody persistence and safety of a tetravalent meningococcal serogroups A, C, W-135 and Y tetanus toxoid conjugate vaccine in children aged 2–10 years**

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Timo Vesikari,<sup>1,\*</sup> Aino Forstén,<sup>1</sup> Dominique Boutriau,<sup>2</sup> Véronique Bianco,<sup>2</sup> Marie Van der Wielen<sup>2</sup> and Jacqueline M. Miller<sup>3</sup>

# rSBA MenA

Antibody	Group	Timing	N	% ≥1:8 (95% CI)	% ≥ 1:128 (95% CI)	GMT (95% CI)
rSBA-MenA	ACWY-TT	Pre	185	67.0 (59.7 – 73.7)	51.9 (44.4 – 59.3)	57.9 (43.3 – 77.5)
		Month 1	225	100 (98.4 – 100)	99.6 (97.5 – 100)	7300.9* (6586.0 – 8093.4)
		Year 1	216	99.5* (97.4 – 100)	99.5* (97.4 – 100)	2448.1* (2149.6 – 2788.1)
		Year 2	208	100* (98.2 – 100)	99.0* (96.6 – 99.9)	1333.4* (1181.9 – 1504.2)
		Year 3	192	100* (98.1 – 100)	99.0* (96.3 – 99.9)	1184.2* (1054.2 – 1330.3)
	Men-PS	Pre	62	64.5 (51.3 – 76.3)	51.6 (38.6 – 64.5)	58.2 (33.8 – 100.1)
		Month 1	75	100 (95.2 – 100)	100 (95.2 – 100)	2033.4 (1667.1 – 2480.2)
		Year 1	71	90.1 (80.7 – 95.9)	80.3 (69.1 – 88.8)	358.5 (230.2 – 558.4)
		Year 2	56	91.1 (80.4 – 97.0)	75.0 (61.6 – 85.6)	202.5 (135.3 – 303.0)
		Year 3	34	91.2 (76.3 – 98.1)	79.4 (62.1 – 91.3)	218.8 (128.9 – 371.5)

# rSBA MenC

Antibody	Group	Timing	N	% ≥1:8 (95% CI)	% ≥ 1:128 (95% CI)	GMT (95% CI)
rSBA-MenC	ACWY-TT	Pre	212	62.7 (55.8 – 69.3)	27.8 (21.9 – 34.4)	33.5 (26.0 – 43.1)
		Month 1	225	100 (98.4 – 100)	99.6* (97.5 – 100)	2435.3* (2105.8 – 2816.3)
		Year 1	215	99.5* (97.4 – 100)	89.3* (84.4 – 93.1)	489.5* (419.5 – 571.1)
		Year 2	210	98.6* (95.9 – 99.7)	75.7* (69.3 – 81.4)	256.0* (213.9 – 306.2)
		Year 3	192	98.4* (95.5 – 99.7)	72.9 (66.0 – 79.1)	244.3 (200.8 – 297.3)
	Men-PS	Pre	70	51.4 (39.2 – 63.6)	27.1 (17.2 – 39.1)	24.1 (15.2 – 38.2)
		Month 1	74	100 (95.1 – 100)	94.6 (86.7 – 98.5)	750.2 (555.2 – 1013.7)
		Year 1	65	80.0 (68.2 – 88.9)	58.5 (45.6 – 70.6)	113.5 (67.3 – 191.5)
		Year 2	59	66.1 (52.6 – 77.9)	45.8 (32.7 – 59.2)	59.9 (33.0 – 108.7)
		Year 3	37	83.8 (68.0 – 93.8)	67.6 (50.2 – 82.0)	163.5 (83.8 – 319.2)

# rSBA MenW

Antibody	Group	Timing	N	% ≥1:8 (95% CI)	% ≥ 1:128 (95% CI)	GMT (95% CI)
rSBA-MenW-135	ACWY-TT	Pre	199	60.3 (53.1 – 67.2)	45.2 (38.2 – 52.4)	43.1 (32.4 – 57.4)
		Month 1	225	100 (98.4 – 100)	100 (98.4 – 100)	11777.0* (10666.2 – 13003.5)
		Year 1	216	100 (98.3 – 100)	99.1* (96.7 – 99.9)	2983.3* (2628.2 – 3386.3)
		Year 2	210	99.5* (97.4 – 100)	99.0* (96.6 – 99.9)	1298.0* (1135.5 – 1483.7)
		Year 3	196	100* (98.1 – 100)	98.0* (94.9 – 99.4)	1737.1* (1503.8 – 2006.7)
	Men-PS	Pre	68	57.4 (44.8 – 69.3)	35.3 (24.1 – 47.8)	40.1 (23.9 – 67.3)
		Month 1	75	100 (95.2 – 100)	100 (95.2 – 100)	2186.3 (1723.1 – 2773.9)
		Year 1	75	100 (95.2 – 100)	93.3 (85.1 – 97.8)	463.0 (367.4 – 583.5)
		Year 2	54	85.2 (72.9 – 93.4)	68.5 (54.4 – 80.5)	144.0 (90.1 – 230.2)
		Year 3	35	82.9 (66.4 – 93.4)	60.0 (42.1 – 76.1)	112.9 (59.9 – 212.6)

# rSBA MenY

Antibody	Group	Timing	N	% ≥1:8 (95% CI)	% ≥ 1:128 (95% CI)	GMT (95% CI)
rSBA-MenY	ACWY-TT	Pre	219	67.1 (60.5 – 73.3)	44.7 (38.0 – 51.6)	57.3 (43.7 – 75.2)
		Month 1	225	100 (98.4 – 100)	99.6 (97.5 – 100)	6641.4* (6044.3 – 7297.4)
		Year 1	216	100* (98.3 – 100)	99.5* (97.4 – 100)	2172.1* (1939.6 – 2432.5)
		Year 2	210	100* (98.3 – 100)	99.5* (97.4 – 100)	1530.2* (1339.2 – 1748.4)
		Year 3	195	100* (98.1 – 100)	100* (98.1 – 100)	1551.6* (1381.2 – 1743.1)
	Men-PS	Pre	70	60.0 (47.6 – 71.5)	40.0 (28.5 – 52.4)	45.5 (26.8 – 77.0)
		Month 1	75	100 (95.2 – 100)	97.3 (90.7 – 99.7)	1409.9 (1085.9 – 1830.5)
		Year 1	71	90.1 (80.7 – 95.9)	78.9 (67.6 – 87.7)	332.4 (213.5 – 517.7)
		Year 2	55	74.5 (61.0 – 85.3)	54.5 (40.6 – 68.0)	96.9 (54.1 – 173.6)
		Year 3	37	81.1 (64.8 – 92.0)	51.4 (34.4 – 68.1)	103.8 (54.3 – 198.3)

# 12 ay- 10 yaş 5 yıllık takip sonuçları

RESEARCH PAPER

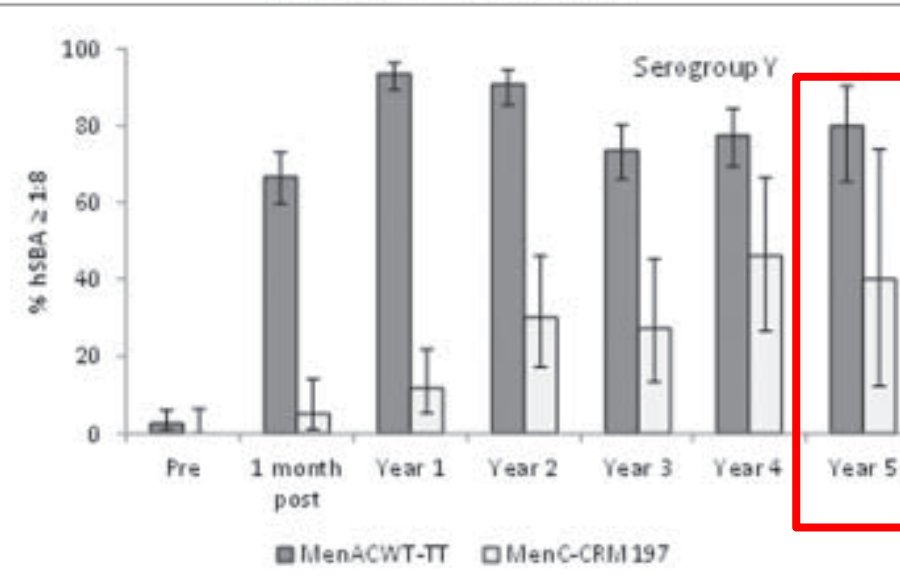
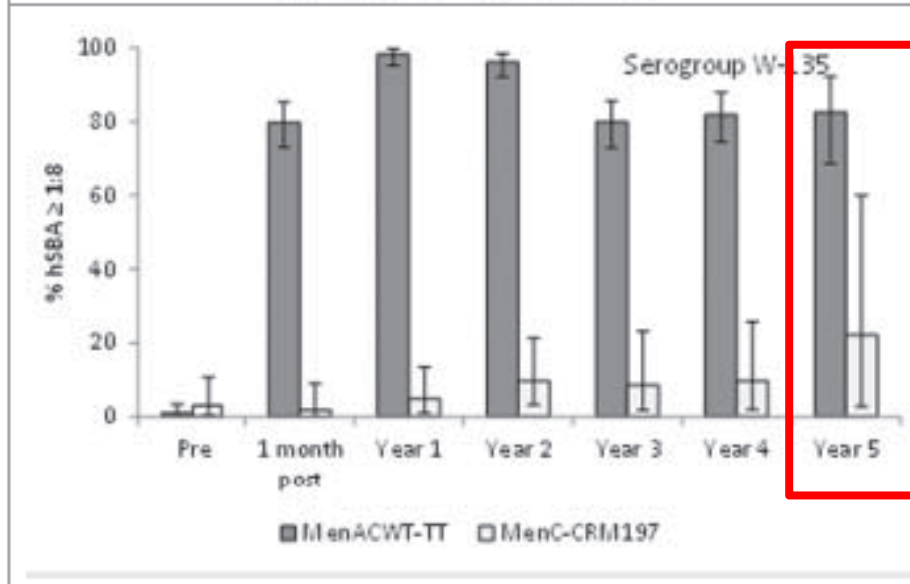
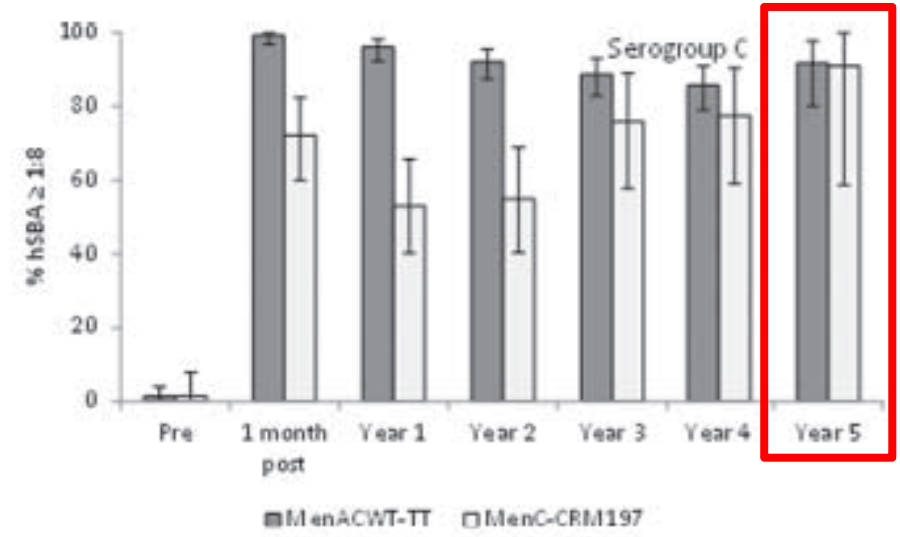
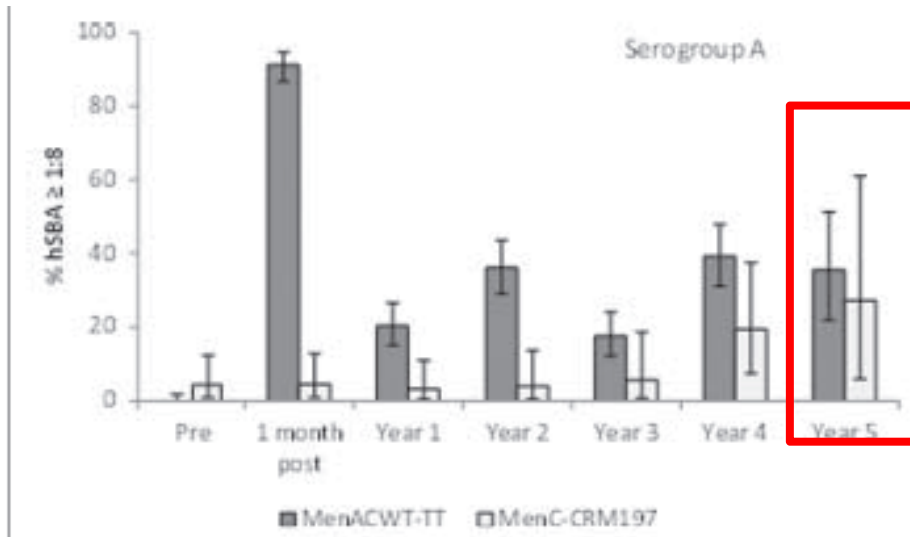
Human Vaccines & Immunotherapeutics 12:1, 132–139; January 2016; Published with license by Taylor & Francis Group, LLC

## Antibody persistence up to 5 years after vaccination of toddlers and children between 12 months and 10 years of age with a quadrivalent meningococcal ACWY-tetanus toxoid conjugate vaccine

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Timo Vesikari<sup>1,\*</sup>, Aino Forsten<sup>1</sup>, Veronique Bianco<sup>2</sup>, Marie Van der Wielen<sup>2</sup>, and Jacqueline M Miller<sup>3</sup>

# % hSBA $\geq$ 1:8



## Antikor yanıtının devamı, tek doz yeterli mi?

This study found that antibody persistence 5 years after MenACWY-TT vaccination in infancy did not differ substantially between children who received 1 or 2 doses, with the exception of serogroup W. Exploratory analyses found that the percentages of children with hSBA-MenW titers  $\geq 4$  and  $\geq 8$  and GMTs were higher in the ACWY-2 group than in the ACWY-1 group. We observed no other potentially significant differences with respect to antibody persistence of serogroups A, C and Y. Overall, 5 years after primary vaccination with MenACWY-TT, there was no clear evidence of benefit of receiving 2 versus 1 dose of vaccine in infancy.

**2 dozun daha faydalı olacağına dair bilimsel kanıt yok**



**TABLE 3.** Percentage of Children with hSBA Titers  $\geq 4$  and  $\geq 8$  at 1 Month After the First dose, 1 Month After the Second Dose and Years 1, 3 and 5 (According to Protocol Immunogenicity Cohorts for Primary Vaccination, Persistence at Year 1, Persistence at Year 3 and Persistence at Year 5)

Antibody	Estimate	Timing	ACWY-1		ACWY-2	
			N	% (95% CI)	N	% (95% CI)
MenA	% $\geq 4$	P1	132	87.1 [80.2–92.3]	128	70.3 [61.6–78.1]
		P2	NA	NA	138	88.4 [81.9–93.2]
		Year 1	102	22.5 [14.9–31.9]	108	26.9 [18.8–36.2]
		Year 3	82	17.1 [9.7–27.0]	96	19.8 [12.4–29.2]
		Year 5	63	31.7 [20.6–44.7]	71	38.0 [26.8–50.3]
	% $\geq 8$	P1	132	79.5 [71.7–86.1]	128	63.3 [54.3–71.6]
		P2	NA	NA	138	88.4 [81.9–93.2]
		Year 1	102	20.6 [13.2–29.7]	108	25.9 [18.0–35.2]
		Year 3	82	17.1 [9.7–27.0]	96	18.7 [9.8–25.6]
		Year 5	63	31.7 [20.6–44.7]	71	38.0 [26.8–50.3]
MenC	% $\geq 4$	P1	130	94.6 [89.2–97.8]	127	90.6 [84.1–95.0]
		P2	NA	NA	137	100 [97.3–100]
		Year 1	104	87.5 [79.6–93.2]	113	91.2 [84.3–95.7]
		Year 3	81	72.8 [61.8–82.1]	94	73.4 [63.3–82.0]
		Year 5	60	78.3 [65.8–87.9]	71	78.9 [67.6–87.7]
	% $\geq 8$	P1	130	94.6 [89.2–97.8]	127	90.6 [84.1–95.0]
		P2	NA	NA	137	100 [97.3–100]
		Year 1	104	87.5 [79.6–93.2]	113	91.2 [84.3–95.7]
		Year 3	81	70.4 [59.2–80.0]	94	72.3 [62.2–81.1]
		Year 5	60	75.0 [62.1–85.3]	71	74.6 [62.9–84.2]
MenW-135	% $\geq 4$	P1	118	53.4 [44.0–62.6]	117	20.5 [13.6–29.0]
		P2	NA	NA	143	99.3 [96.2–100]
		Year 1	104	89.4 [81.9–94.6]	112	99.1 [95.1–100]
		Year 3	86	62.8 [51.7–73.0]	97	84.5 [75.8–91.1]
		Year 5	61	65.6 [52.3–77.3]	72	86.1 [75.9–93.1]
	% $\geq 8$	P1	118	38.8 [41.5–86.2]	117	18.8 [12.2–27.1]
		P2	NA	NA	143	99.3 [96.2–100]
		Year 1	104	89.4 [81.9–94.6]	112	99.1 [95.1–100]
		Year 3	86	62.8 [51.7–73.0]	97	84.5 [75.8–91.1]
		Year 5	61	65.6 [52.3–77.3]	72	86.1 [75.9–93.1]
MenY	% $\geq 4$	P1	132	59.8 [51.0–68.3]	131	39.7 [31.3–48.6]
		P2	NA	NA	146	99.3 [96.2–100]
		Year 1	110	80.9 [72.3–87.8]	120	92.5 [86.2–96.5]
		Year 3	85	62.4 [51.2–72.6]	95	62.1 [51.6–71.9]
		Year 5	50	64.0 [49.2–77.1]	63	77.8 [65.5–87.3]
	% $\geq 8$	P1	132	56.1 [47.2–64.7]	131	37.4 [29.1–46.3]
		P2	NA	NA	146	99.3 [96.2–100]
		Year 1	110	80.0 [71.3–87.0]	120	92.5 [86.2–96.5]
		Year 3	85	62.4 [51.2–72.6]	95	62.1 [51.6–71.9]
		Year 5	50	64.0 [49.2–77.1]	63	77.8 [65.5–87.3]

# Aşının yan etkileri

## **SİSTEMİK İSTENMEYEN ETKİLER**

- **12-23 ay: irritabilite, halsizlik, ateş, iştahsızlık**
- **2-5 yaş yaş: halsizlik, irritabilite, ateş, iştahsızlık**
- **6-10 yaş: halsizlik, baş ağrısı, GIS bulguları, ateş**
- **11-17 yaş: halsizlik, baş ağrısı, GIS bulguları, ateş**
- **18-55 yaş: baş ağrısı,halsizlik, GIS bulguları, ateş**

**Aşının diğer aşılarla beraber kullanımı**

- Hep A/B
- MMRV
- Influenza
- PCV10-13
- DTPa-HBV-IPV/Hib



Contents lists available at ScienceDirect

## Vaccine

journal homepage: [www.elsevier.com/locate/vaccine](http://www.elsevier.com/locate/vaccine)



### A B S T R A C T

Tetravalent meningococcal serogroups ACWY conjugate vaccines will provide an advantage to those at most risk of invasive meningococcal disease; namely young children. Co-administration of ACWY-TT with DTaP-HBV-IPV/Hib was assessed in a randomized trial in 793 children aged 12–23 months. Pre-specified criteria for non-inferiority of immunogenicity following co-administration versus separate ACWY-TT and DTaP-HBV-IPV/Hib administration were reached. One month post-vaccination,  $\geq 97.3\%$  of ACWY-TT vaccinees had rSBA titres  $\geq 1:8$  (all serogroups). Seroprotection/seropositivity rates against DTaP-HBV-IPV/Hib antigens were  $>98.2\%$ . The safety profile of co-administration was similar to that of DTaP-HBV-IPV/Hib alone. ACWY-TT and DTaP-HBV-IPV/Hib co-administration during the second year would facilitate introduction of ACWY-TT into routine toddler vaccination schedules.

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**DaBT-IPV/Hib ile beraber yapılması güvenilir**



Contents lists available at ScienceDirect

Vaccine

journal homepage: [www.elsevier.com/locate/vaccine](http://www.elsevier.com/locate/vaccine)

Tetravalent meningococcal serogroups A, C, W-135 and Y conjugate vaccine is well tolerated and immunogenic when co-administered with measles–mumps–rubella–varicella vaccine during the second year of life: An open, randomized controlled trial

**Table 5**

rSBA geometric mean titres 42 days after the first vaccination in each treatment group (ATP immunogenicity cohort).

Group Serogroup	ACWY+MMRV		ACWY-TT		MenC	
	N	GMT [95% CI]	N	GMT [95% CI]	N	GMT [95% CI]
A	360	2085.9 [1905.3; 2283.6]	354	2205.0 [2007.8; 2421.6]	51	24.3 [13.4; 44.1]
C	357	519.0* [470.9; 571.9]	354	477.6* [437.3; 521.6]	121	212.3 [170.0; 265.2]
W-135	360	2055.8 [1871.0; 2258.9]	354	2681.7 [2453.1; 2931.6]	58	25.1 [14.6; 43.1]
Y	359	2282.4 [2051.3; 2539.5]	354	2729.4 [2472.7; 3012.8]	59	31.4 [18.4; 53.6]

N = number of subjects with results available. 95% CI = 95% confidence intervals. GMT = geometric mean antibody titre calculated on all subjects.

\* Statistically significantly higher compared to MenC group (exploratory analysis based on adjusted GMT ratio).

**KKK aşısı ile yapılması güvenlidir**

# 13 bileşenli pnömokok aşısı

- MenACWY-TT aşısı ile birlikte yapılabilir...
- EMA, Ruhsat onayı 17 Kasım 2016



# EMA, Nimenrix infant endikasyonu için pozitif görüş bildirdi

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EUROPEAN MEDICINES AGENCY  
SCIENCE MEDICINES HEALTH

10 November 2016  
EMA/CHMP/512584/2016  
Committee for Medicinal Products for Human Use (CHMP)

## Summary of opinion<sup>1</sup> (post authorisation)

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### Nimenrix

Meningococcal group A, C, W-135 and Y conjugate vaccine

On 10 November 2016, the Committee for Medicinal Products for Human Use (CHMP) adopted a positive opinion recommending a change to the terms of the marketing authorisation for the medicinal product Nimenrix. The marketing authorisation holder for this medicinal product is Pfizer Limited.

The CHMP adopted an extension to the existing indication as follows<sup>2</sup>:

"Nimenrix is indicated for active immunisation of individuals from the age of 6 weeks ~~12 months and above~~ against invasive meningococcal diseases caused by *Neisseria meningitidis* group A, C, W-135, and Y".

Detailed recommendations for the use of this product will be described in the updated summary of product characteristics (SmPC), which will be published in the revised European public assessment report (EPAR), and will be available in all official European Union languages after a decision on this change to the marketing authorisation has been granted by the European Commission.

# Sonuç

- Türkiye için Serogrup A/C/Y/W konjuge aşıları uygun aşılardır
- En çok olgular 5 yaş altı grupta görülüyor bu nedenle küçük yaş grubunda aşılama önemli
- MenACWY-TT Aşısı 1 yaş üstü çocuklarda güvenle uygulanabilir
- Tek doz uygulamada antikor yanıtı 5 yıl sürmektedir
- Diğer aşılarla birlikte kullanılabilir
- İleri çalışmalar gereklidir