



# FOLİKÜLER TİROİD NEOPLAZİLERİNDE HBME-1, GALECTİN-3, CK19 VE CD56 İMMUNPROFİLİNİN DEĞERLENDİRİLMESİ

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# Giriş

- Tiroid kanserleri en sık görülen endokrin neoplazilerdir
  - Foliküler epitel kaynaklı kanserler (~ %95)
    - İyi diferansiye tiroid karsinomları (papiller, foliküler)
    - Az diferansiye tiroid karsinomu
    - Anaplastik tiroid karsinomu
  - Parafoliküler c-hücre kaynaklı kanserler
    - Medüller tiroid karsinomu (~ %5)
- Görülme sıklığı ↑ ↑ ↑
  - Küçük çaplı kanserlerin tanınması

- Albores-Saavedra J, Henson DE, Glazer E, Schwartz AM. Changing patterns in the incidence and survival of thyroid cancer with follicular phenotypepapillary, follicular, and anaplastic: a morphological and epidemiological study. *Endocr Pathol* 2007;18(1):1–7. Spring. Reynolds RM, Weir J, Stockton DL, Brewster DH, Sandeep TC, Strachan MW.
- Changing trends in incidence and mortality of thyroid cancer in Scotland. *Clin Endocrinol (Oxf)* 2005 Feb;62(2):156–62.
- Cassol, C. A., & Asa, S. L. (2011). Molecular pathology of thyroid cancer. *Diagnostic histopathology*, 17 (3), 124-139.



# Giriş

- Tiroid lezyonlarının tanısında altın standart ---- *hematoksilen ve eozin (H&E)*
- Foliküler lezyonlar ve foliküler varyant papiller tiroid karsinomu (FVPTK) arasında morfolojik örtüşmeler (+) ---- *morfolojik özelliklere dayanarak tanı zor olabilir*
- **HBME-1, CK19, Galectin-3, CD56**, p63, CK903, CITED1, Ret onkoproteini, CD44, CD57, Siklin D1, p27,.....



# Amaç

- Bölümümüzde tanı almış foliküler neoplazi olgularında HBME-1, Galectin-3, CK19, CD56 ekspresyon dağılımlarını ortaya koymak



# Gereç-Yöntem

Bu çalışmada;

- 18 foliküler adenom
- 20 minimal invaziv foliküler karsinom
- 9 geniş invaziv foliküler karsinom
- 24 foliküler varyant papiller tiroid karsinomu

vakasına immunhistokimyasal olarak HBME-1, Galectin-3, CK19, CD56 uygulanmıştır

Seçilen vakalar ve immunhistokimya sonuçları iki araştırmacı tarafından değerlendirilmiştir (BE, FA)

<b>Antikor</b>	<b>Klon</b>	<b>Dilüsyon</b>	<b>Marka</b>
HBME-1	HBME-1	1:50	Thermo Scientific
Galectin-3	9C4	1:100	Novocastra
CK 19	A53-B/A2.26	1:300	Thermo Scientific
CD 56	123C3	1:100	Genemed



# Gereç-Yöntem

- **Pozitif boyanma:**
  - **HBME-1: lateral ve abluminal yüzeylerde membranöz boyanma ± sitoplazmik boyanma<sup>1</sup>**
  - **Galectin-3: sitoplazmik ± nükleer boyanma<sup>2</sup>**
  - **CK19: membranöz ± sitoplazmik boyanma<sup>3</sup>**
  - **CD56: membranöz ± sitoplazmik boyanma<sup>4</sup>**
- **>%10 boyanma pozitif kabul edildi (HBME-1, Galectin-3, CK19)**
- **CD56: <%10 pozitif --- malign profil**

1. Ito, Y., Yoshida, H., Tomoda, C., Miya, A., Kobayashi, K., Matsuzuka, F., Miyauchi, A. (2005). HBME-1 expression in follicular tumor of the thyroid: an investigation of whether it can be used as a marker to diagnose follicular carcinoma. *Anticancer research*, 25(1A), 179-182.
2. Liu, J., Singh, B., Tallini, G., Carlson, D. L., Katabi, N., Shaha, A., Ghossein, R. A. (2006). Follicular variant of papillary thyroid carcinoma. *Cancer*, 107(6), 1255-1264.
3. Saleh, H. A., Feng, J., Tabassum, F., Al-Zohaili, O., Husain, M., & Giorgadze, T. (2009). Differential expression of galectin-3, CK19, HBME1, and Ret oncoprotein in the diagnosis of thyroid neoplasms by fine needle aspiration biopsy. *Cytojournal*, 6(1), 18.
4. Park, W. Y., Jeong, S. M., Lee, J. H., Kang, H. J., Sin, D. H., Choi, K. U., Lee, C. H. (2009). Diagnostic value of decreased expression of CD56 protein in papillary carcinoma of the thyroid gland. *Basic and Applied Pathology*, 2(2), 63-68.



H&E

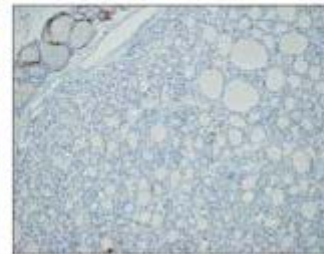
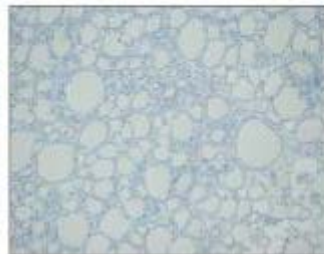
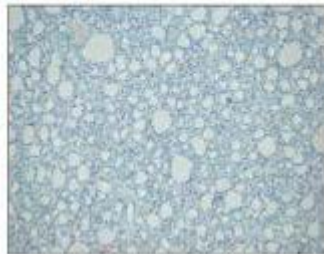
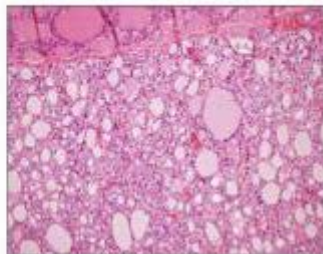
HBME-1

Galectin 3

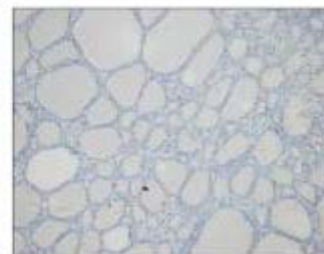
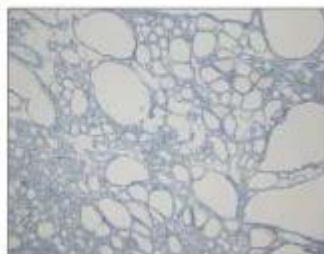
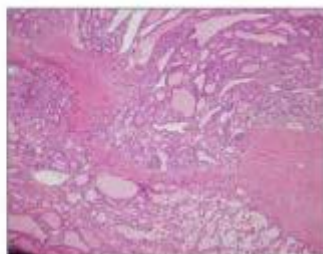
CK19

CD56

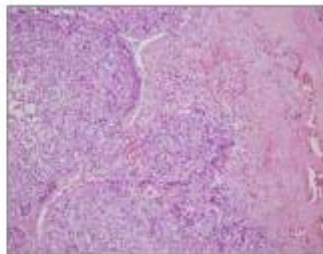
FA



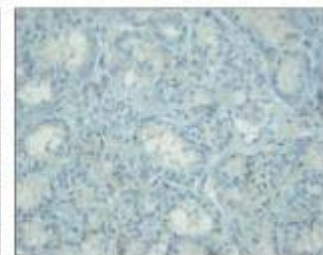
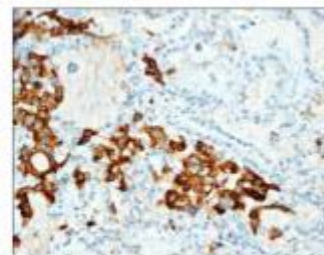
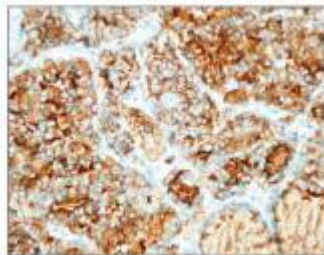
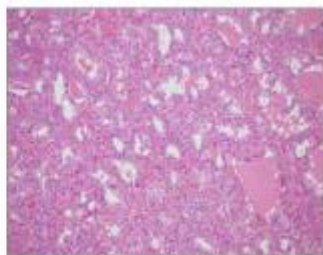
Min. inv. FK



Gen. inv. FK



FVPTK





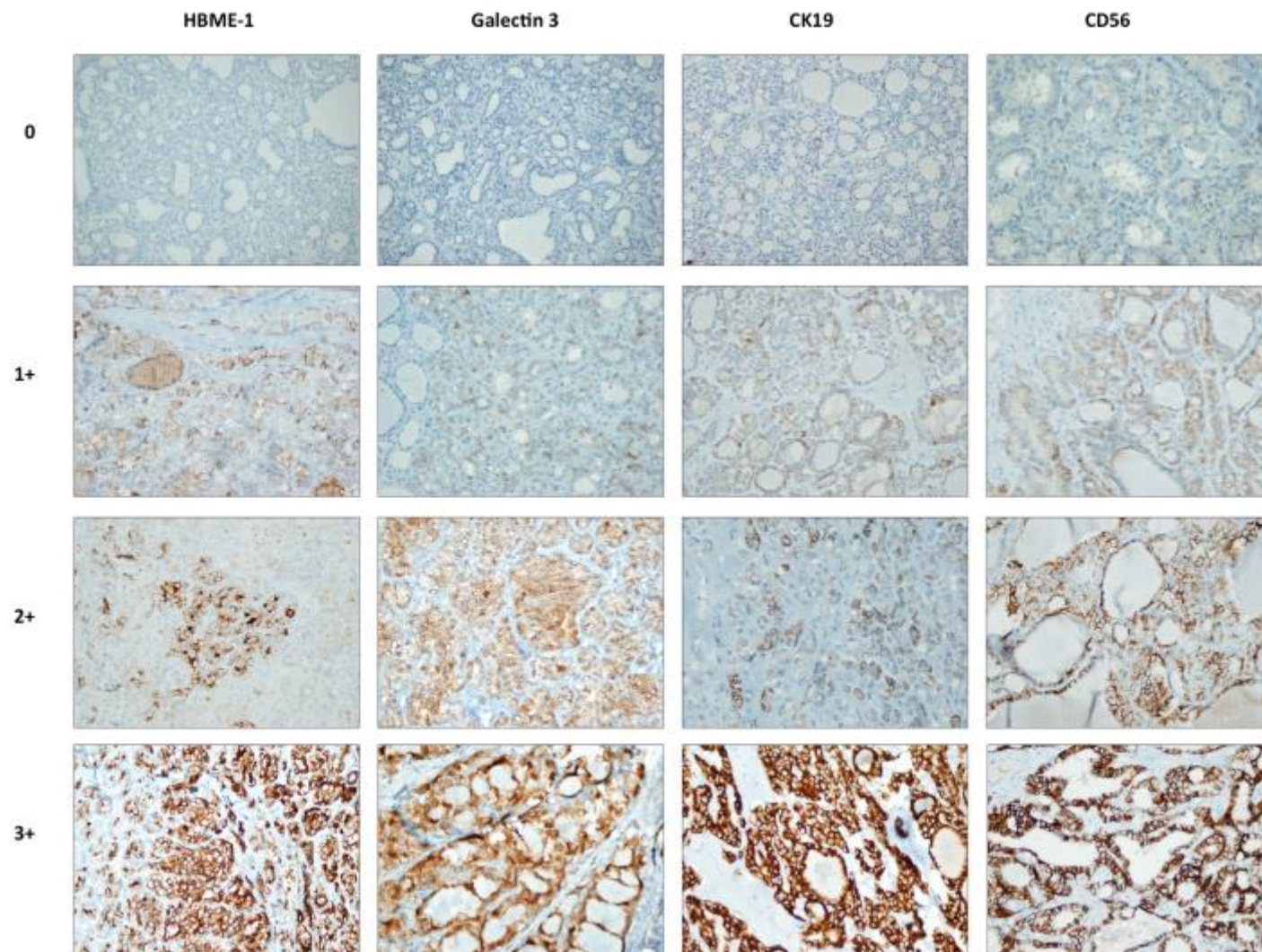
# Gereç-Yöntem

- Boyanma yaygınlıkları skorlandı
  - %10-%25 ----1
  - %26-%50 ----2
  - %51-%75 ----3
  - %76-%100 ----4





# Gereç-Yöntem





# Gereç-Yöntem

- İstatiksel yöntem
  - Tanımlayıcı özellikler
  - Sensitivite/spesifisite
  - Ki kare testi ( $p < 0,005$  anlamlı)
- Analizlerde
  - SPSS 22.0 (SPSS Inc.)
  - Microsoft Excel



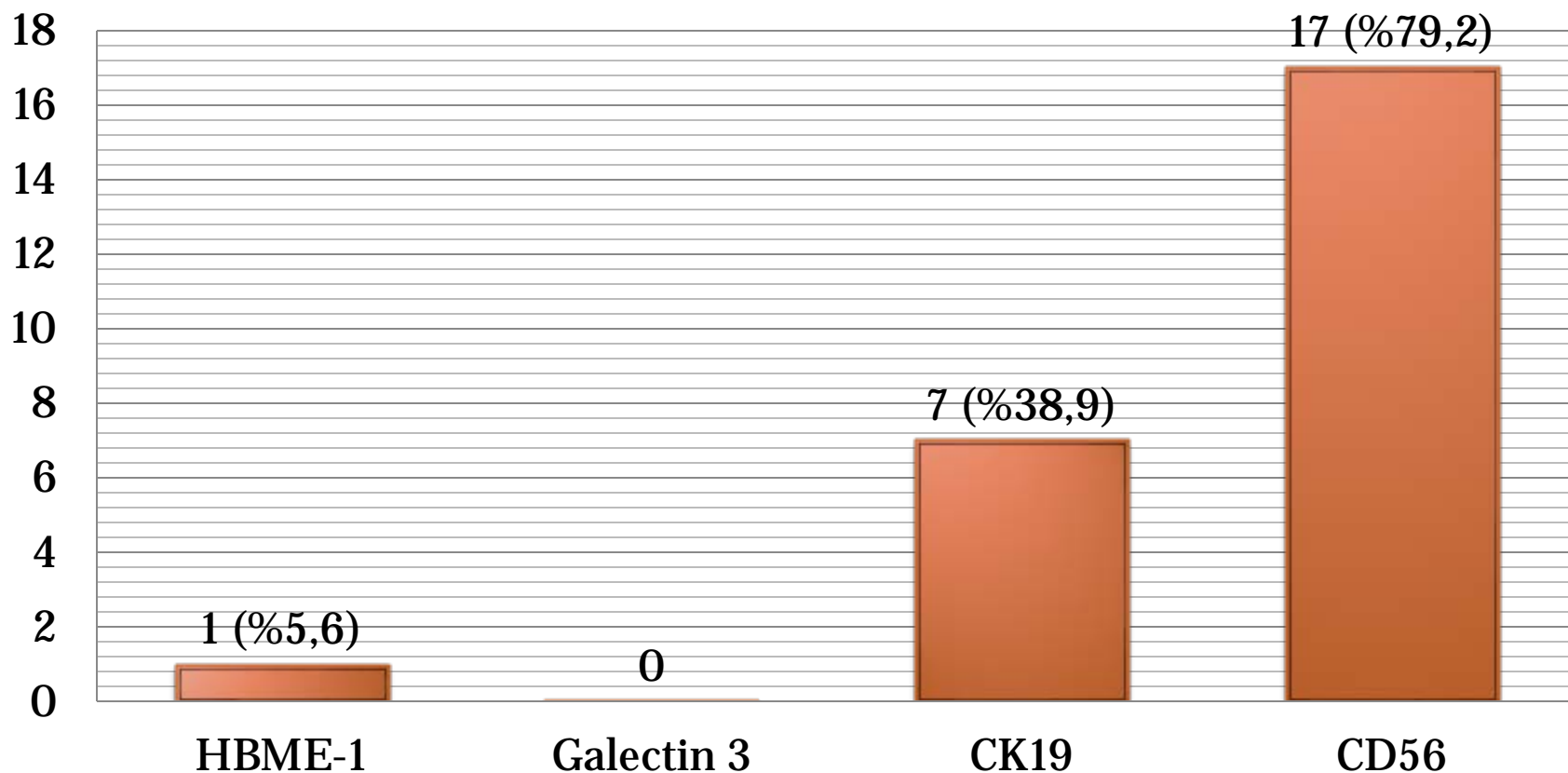
# Bulgular

	<b>FA</b>	<b>Min. inv. FK</b>	<b>Gen. inv. FK</b>	<b>FVPTK</b>	<b>Toplam</b>
<b>F/M</b>	<b>13/5</b> (%72,2/%27,8)	<b>16/4</b> (%80/%20)	<b>7/2</b> (%77,8/%22,7)	<b>23/1</b> (%95,8/%4,2)	<b>59/12</b> (%83,1/%16,9)
<b>Ort. yaş</b>	<b>48,3 (22-66)</b>	<b>48,6 (29-74)</b>	<b>54 (34-69)</b>	<b>39,5 (19-76)</b>	<b>46,1 (19-76)</b>
<b>Tm çapı</b>	<b>2,6 (0,9-5)</b>	<b>2,9 (1,4-5,3)</b>	<b>4,1 (2-8)</b>	<b>2,6 (0,9-6,5)</b>	<b>2,9 (0,9-8)</b>



# Bulgular

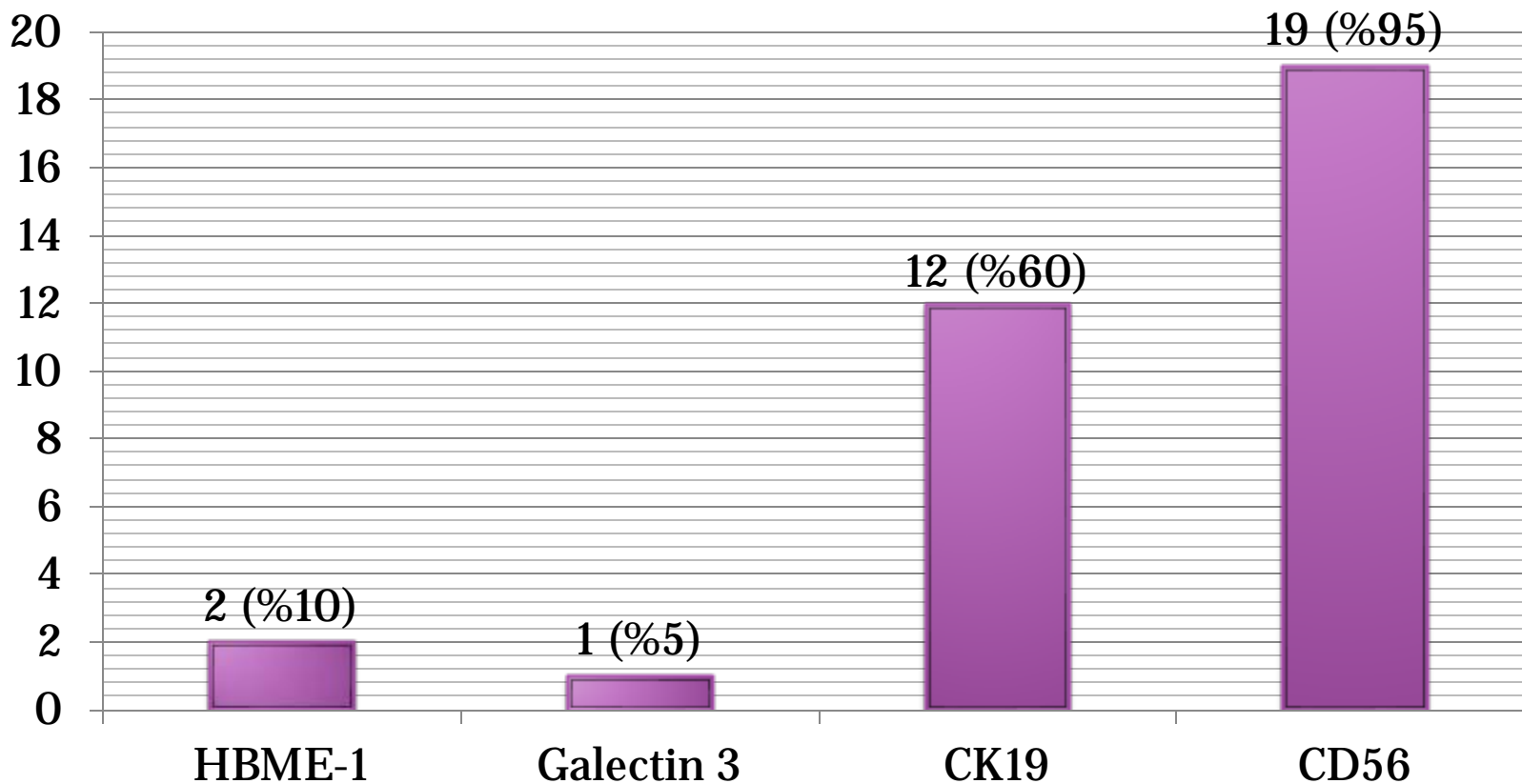
## Foliküler adenomlarda immunprofil





# Bulgular

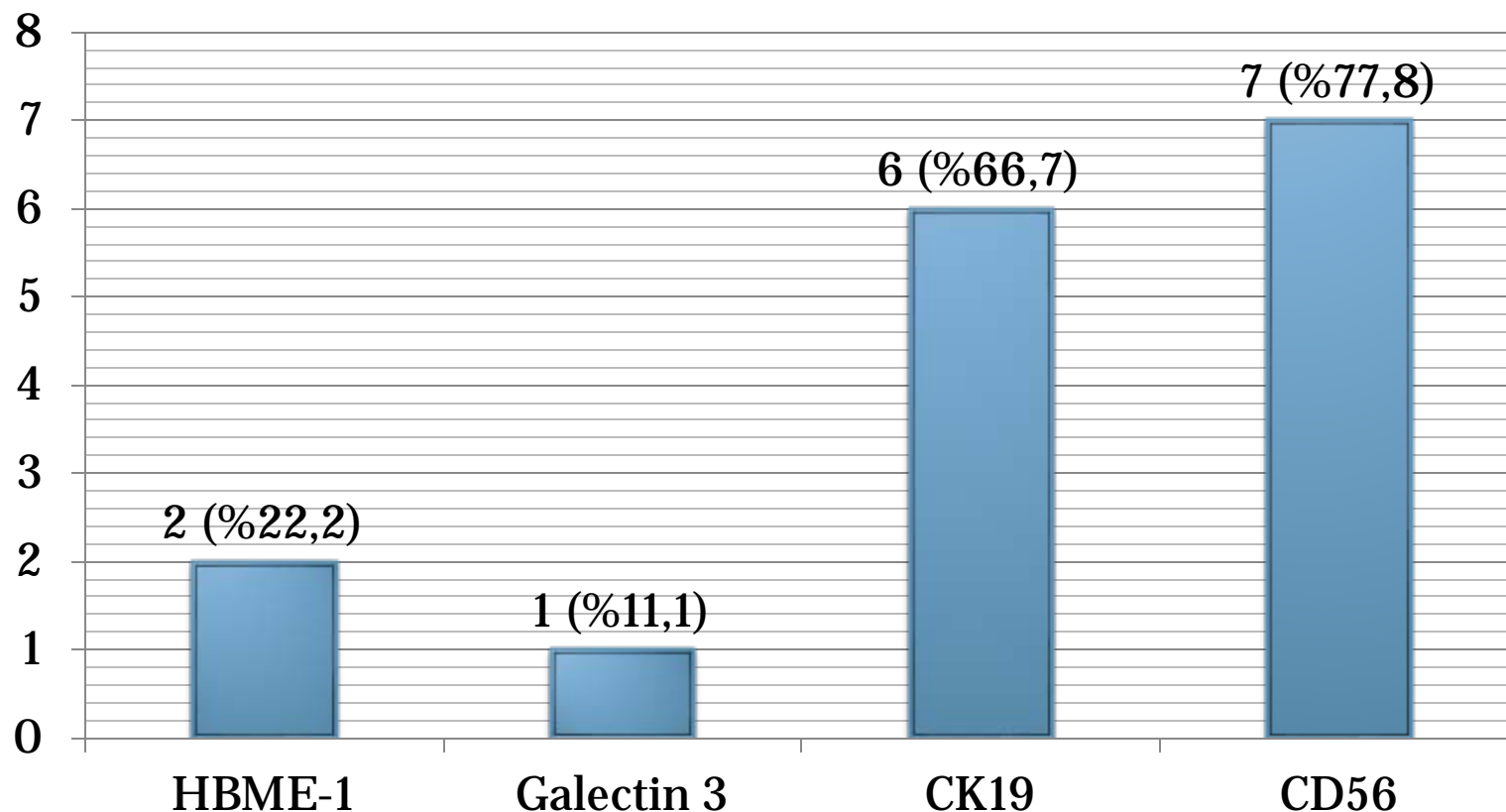
## Minimal invaziv foliküler karsinomlarda immunprofil





# Bulgular

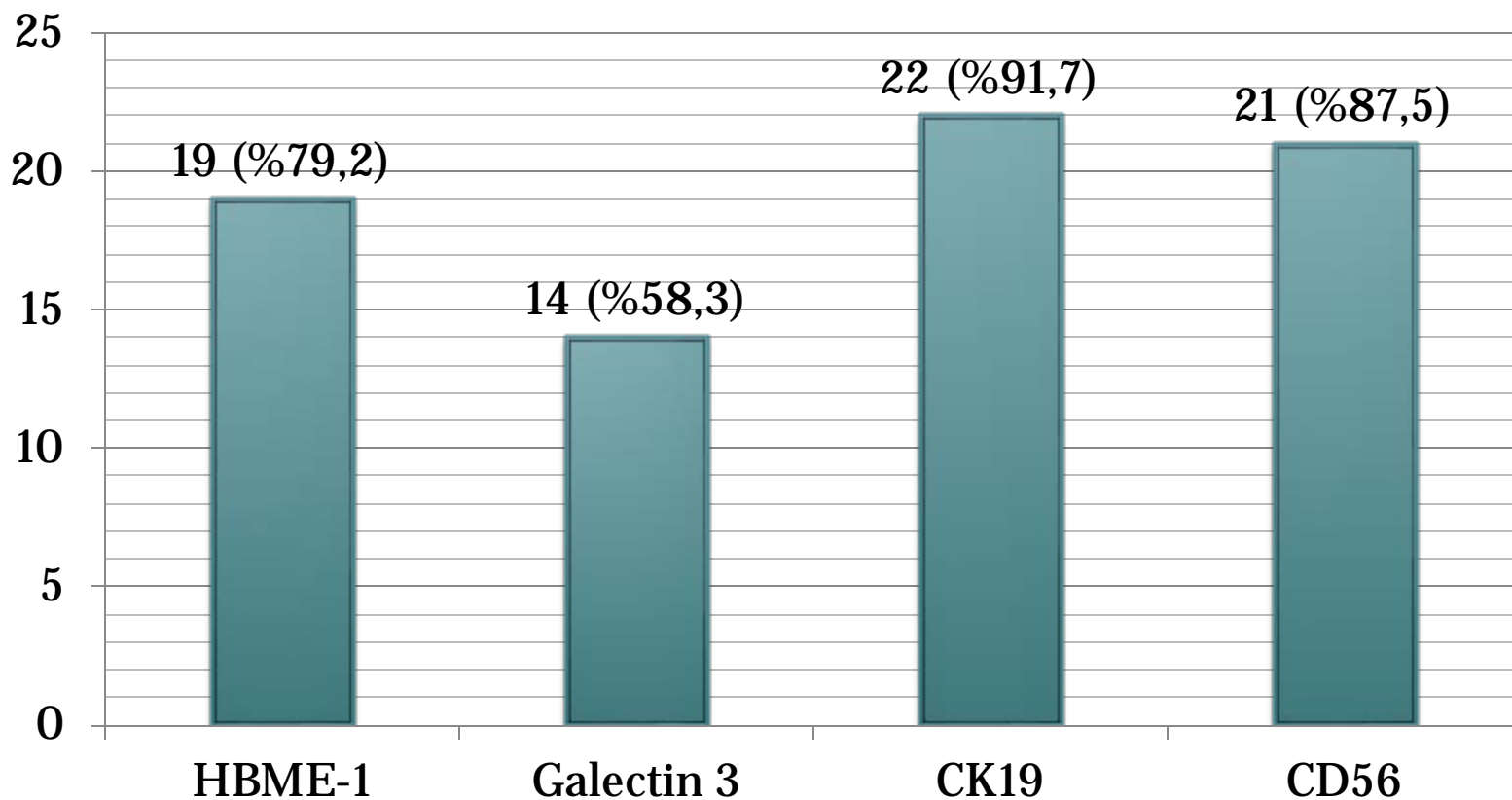
## Geniş invaziv foliküler karsinomlarda immunprofil





# Bulgular

Foliküler varyant papiller tiroid karsinomlarında immunprofil





# Bulgular

	FVPTK	
	sensitivite	spesifisite
<b>HBME-1<sup>+</sup></b>	79,2	89
<b>Galectin-3<sup>+</sup></b>	58,3	95,7
<b>CK19<sup>+</sup></b>	87,5	48,9
<b>CD56<sup>-</sup></b>	12,5	91,5
<b>HBME-1<sup>+</sup>+Galectin-3<sup>+</sup></b>	73,7	95,5
<b>HBME-1<sup>+</sup>+CK19<sup>-</sup></b>	86,4	82,1
<b>HBME-1<sup>+</sup>+CD56<sup>-</sup></b>	62,5	97,5
<b>Galectin-3<sup>+</sup>+CK19<sup>-</sup></b>	82,4	92
<b>Galectin-3<sup>+</sup>+CD56<sup>-</sup></b>	18,2	100
<b>CK19<sup>+</sup>+CD56<sup>-</sup></b>	50	85,2
<b>HBME-1<sup>-</sup>+Galectin-3<sup>-</sup>+CK19<sup>-</sup></b>	82,4	92
<b>HBME-1<sup>-</sup>+Galectin-3<sup>+</sup>+CD56<sup>+</sup></b>	28,6	100
<b>HBME-1<sup>-</sup>+CK19<sup>-</sup>+CD56<sup>+</sup></b>	50	95,8
<b>HBME-1<sup>-</sup>+Galectin-3<sup>-</sup>+CK19<sup>-</sup>+CD56<sup>+</sup></b>	60	100





	FA		Min. inv FK		Gen. inv FK	
	sensitivite	spesifisite	sensitivite	spesifisite	sensitivite	spesifisite
<b>HBME-1<sup>-</sup></b>	94,4	43,4	90	43,1	77,8	35,4
<b>Galectin-3<sup>-</sup></b>	100	29,4	95	24,1	88,9	24,2
<b>CK19<sup>-</sup></b>	61,1	71,6	45	66,7	33,3	62,9
<b>CD56<sup>+</sup></b>	95	11,3	95	11,8	77,8	8,1
<b>HBME-1<sup>-</sup>+Galectin-3<sup>-</sup></b>	100	34,8	94,7	34,1	87,5	27,3
<b>HBME-1<sup>-</sup>+CK19<sup>-</sup></b>	91,7	60,5	81,8	56,4	60	48,9
<b>HBME-1<sup>-</sup>+CD56<sup>+</sup></b>	100	12,5	94,7	10,3	100	9,3
<b>Galectin-3<sup>-</sup>+CK19<sup>-</sup></b>	100	51,6	90	46,9	75	39,5
<b>Galectin-3<sup>-</sup>+CD56<sup>+</sup></b>	100	5,9	100	6,2	100	4,5
<b>CK19<sup>-</sup>+CD56<sup>+</sup></b>	91,7	28,6	90	26,1	60	17,9
<b>HBME-1<sup>-</sup>+Galectin-3<sup>-</sup>+CK19<sup>-</sup></b>	100	51,6	90	46,9	75	39,5
<b>Hbme-1<sup>-</sup>+Galectin-3<sup>+</sup>+CD56<sup>+</sup></b>	100	6,7	100	7,2	100	4,9
<b>HBME-1<sup>-</sup>+CK19<sup>-</sup>+CD56<sup>+</sup></b>	100	21,1	90	15	100	14,8
<b>HBME-1<sup>-</sup>+Galectin-3<sup>-</sup>+CK19<sup>-</sup>+CD56<sup>+</sup></b>	100	11,8	100	10,5	100	8



# Bulgular

HBME-1 ile boyanma yaygınlığının değerlendirilmesi

	-		1+		2+		3+		4+		ort.
	n	%	n	%	n	%	n	%	n	%	
<b>FA</b>	17	94,4	0	0	1	5,6	0	0	0	0	0,1
<b>Min. inv. FK</b>	17	85	1	5	0	0	0	0	1	10	0,5
<b>Gen. inv. FK</b>	7	77,8	1	11,1	0	0	1	11,1	0	0	0,4
<b>FVPTK</b>	5	20,8	2	8,3	5	20,8	3	8,3	10	41,7	2,4
<b>Total</b>	46	64,8	4	5,6	6	8,5	3	4,2	12	16,9	

FVPTK ---- ort: 2,4  
Diğerleri -- ort: 0,3



p=0,0001

Ki kare testi, p<0,05



# Bulgular

HBME-1 ile boyanma yoğunluğunun değerlendirilmesi

	-		1+		2+		3+		ort.
	n	%	n	%	n	%	n	%	
<b>FA</b>	16	88,9	0	0	0	0	2	11,1	0,3
<b>Min. inv. FK</b>	16	80	0	0	3	15	1	5	0,5
<b>Gen. inv. FK</b>	7	77,8	0	0	2	22,2	0	0	0,4
<b>FVPTK</b>	5	20,8	1	4,2	10	41,7	8	33,3	1,9
<b>Total</b>	44	62	1	1,4	15	21,1	11	15,5	

FVPTK ---- ort: 1,9  
Diğerleri -- ort: 0,4



p=0,001

Ki kare testi,  $p < 0,05$



## CD56 ile boyanma yaygınlığının değerlendirilmesi

	-		1+		2+		3+		4+		ort.	p
	n	%	n	%	n	%	n	%	n	%		
<b>FA</b>	1	5,6	0	0	0	0	1	5,6	16	85,9	3,7	0,004
<b>Min. inv. FK</b>	1	5	0	0	1	5	1	5	17	85	3,7	
<b>Gen. inv. FK</b>	2	22,2	2	22,2	0	0	0	0	5	55,6	2,4	
<b>FVPTK</b>	3	12,5	4	16,7	3	12,5	7	29,2	7	29,2	2,5	
<b>Total</b>	7	9,9	6	8,5	4	5,6	9	12,7	45	63,4		

## CD56 ile boyanma yoğunluğunun değerlendirilmesi

	-		1+		2+		3+		ort.	p
	n	%	n	%	n	%	n	%		
<b>FA</b>	1	5,6	0	0	9	50	8	44,4	2,3	0,012
<b>Min. inv. FK</b>	1	5	3	15	3	15	13	65	2,4	
<b>Gen. inv. FK</b>	2	22,2	3	33,3	3	33,3	1	11,1	1,3	
<b>FVPTK</b>	3	12,5	4	16,7	13	54,2	4	16,7	1,8	
<b>Total</b>	7	9,9	10	4,1	28	39,4	26	36,6		

Ki kare testi,  $p < 0,05$

# Tartışma



## HBME-1

Cheung ve ark. --- PTK'ların %55'inde (+)

Rossi ve ark. }  
Saleh ve ark. } malign x benign tiroid  
lezyonu ayırımında  
sensitivitesi yüksek

Ozolins ve ark. }  
Nakamura ve ark. } FPTK x FA ayırımı

## CK19

Raphael ve ark. }  
Zhu ve ark }  
Atik ve ark. } PTK x benign lezyon  
ayırımında faydalı

Fonseca ve ark. }  
Miettinen ve ark. } Foliküler  
neoplazilerde de  
pozitiflik söz konusu

## Galectin-3

Saggiorato ve ark. ---- malign x benign  
tiroid lezyonu ayırımında sensitivitesi  
yüksek

Park ve ark. --- foliküler karsinomlarda  
ekspresyon (+)

## CD56

Ozolins ve ark. }  
Scarpino ve ark. } PTK'larda (-)

El Demellawy ve ark. --- PTK x foliküler  
lezyon ayırımında faydalı

**Etem ve ark. --- Diğer foliküler  
neoplazilerle FVPTK arasında  
anlamli fark yok**



# Sonuç

- HE inceleme altın standart ---- ancak ayırıcı tanıda destek
- HBME-1 ile boyanma tek başına FVPTK tanısı koymada yetersiz



İmmun panele  
Galectin-3, CK19 ve CD56  
eklenebilir

***TEŞEKKÜRLER***