

Variable	Coordinates of ROC curve					
	positive if ≥	sensitivity	1 - specificity	specificity	sensitivity + specificity	Youden
Overall CD3+ TIL	-0,5000	1,000	1,000	0,000	1,000	0,000
	0,6250	0,967	0,948	0,052	1,018	0,018
	0,8750	0,900	0,866	0,134	1,034	0,034
	1,1250	0,867	0,835	0,165	1,032	0,032
	1,3750	0,833	0,814	0,186	1,019	0,019
	1,6250	0,833	0,794	0,206	1,040	0,040
	1,8750	0,800	0,784	0,216	1,016	0,016
	2,2500	0,733	0,753	0,247	0,981	-0,019
	2,6250	0,733	0,742	0,258	0,991	-0,009
	2,8750	0,700	0,742	0,258	0,958	-0,042
	3,2500	0,633	0,701	0,299	0,932	-0,068
	3,6250	0,633	0,670	0,330	0,963	-0,037
	3,8750	0,633	0,649	0,351	0,984	-0,016
	4,2500	0,600	0,619	0,381	0,981	-0,019
	4,7500	0,600	0,598	0,402	1,002	0,002
	5,2500	0,600	0,546	0,454	1,054	0,054
	5,7500	0,600	0,536	0,464	1,064	0,064
	6,2500	0,600	0,474	0,526	1,126	0,126
	6,7500	0,567	0,474	0,526	1,092	0,092
	7,2500	0,567	0,433	0,567	1,134	0,134
	7,6250	0,500	0,402	0,598	1,098	0,098
	8,1250	0,500	0,392	0,608	1,108	0,108
	8,7500	0,500	0,361	0,639	1,139	0,139
	9,5000	0,500	0,351	0,649	1,149	0,149
	10,1250	0,467	0,320	0,680	1,147	0,147
	10,6250	0,433	0,320	0,680	1,114	0,114
	11,7500	0,400	0,309	0,691	1,091	0,091
	13,7500	0,367	0,299	0,701	1,068	0,068
	15,5000	0,300	0,237	0,763	1,063	0,063
	16,7500	0,267	0,237	0,763	1,030	0,030
	18,7500	0,233	0,237	0,763	0,996	-0,004
	21,2500	0,133	0,196	0,804	0,937	-0,063
	23,7500	0,067	0,186	0,814	0,881	-0,119
	26,2500	0,067	0,144	0,856	0,922	-0,078
	28,7500	0,033	0,113	0,887	0,920	-0,080
	31,2500	0,000	0,103	0,897	0,897	-0,103
	33,7500	0,000	0,082	0,918	0,918	-0,082
	36,2500	0,000	0,072	0,928	0,928	-0,072
	38,7500	0,000	0,062	0,938	0,938	-0,062
	43,7500	0,000	0,052	0,948	0,948	-0,052
	48,7500	0,000	0,041	0,959	0,959	-0,041
	52,5000	0,000	0,031	0,969	0,969	-0,031
	60,0000	0,000	0,021	0,979	0,979	-0,021
67,5000	0,000	0,010	0,990	0,990	-0,010	
71,0000	0,000	0,000	1,000	1,000	0,000	
Overall CD8+ TIL	-1,0000	1,000	1,000	0,000	1,000	0,000
	0,1250	0,967	0,969	0,031	0,998	-0,002
	0,3750	0,967	0,959	0,041	1,008	0,008
	0,6250	0,900	0,856	0,144	1,044	0,044
	0,8750	0,867	0,794	0,206	1,073	0,073
	1,1250	0,800	0,722	0,278	1,078	0,078
	1,3750	0,767	0,701	0,299	1,066	0,066
	1,6250	0,767	0,660	0,340	1,107	0,107
	1,8750	0,767	0,639	0,361	1,127	0,127
	2,2500	0,767	0,546	0,454	1,220	0,220
	2,6250	0,600	0,546	0,454	1,054	0,054
	2,8750	0,600	0,536	0,464	1,064	0,064
	3,2500	0,600	0,505	0,495	1,095	0,095
	3,6250	0,600	0,464	0,536	1,136	0,136
	3,8750	0,533	0,464	0,536	1,069	0,069
	4,5000	0,467	0,412	0,588	1,054	0,054
	5,1250	0,467	0,381	0,619	1,085	0,085
	5,3750	0,433	0,371	0,629	1,062	0,062
	5,7500	0,400	0,371	0,629	1,029	0,029
	6,5000	0,367	0,361	0,639	1,006	0,006
	7,7500	0,300	0,320	0,680	0,980	-0,020
	9,2500	0,300	0,299	0,701	1,001	0,001
	10,5000	0,233	0,289	0,711	0,945	-0,055
	11,7500	0,200	0,278	0,722	0,922	-0,078
	13,0000	0,167	0,268	0,732	0,899	-0,101
	14,2500	0,167	0,247	0,753	0,919	-0,081
	15,5000	0,100	0,196	0,804	0,904	-0,096
	16,7500	0,100	0,175	0,825	0,925	-0,075
	18,7500	0,100	0,165	0,835	0,935	-0,065
	21,2500	0,033	0,144	0,856	0,889	-0,111
	23,7500	0,000	0,103	0,897	0,897	-0,103
	27,5000	0,000	0,052	0,948	0,948	-0,052
	31,2500	0,000	0,041	0,959	0,959	-0,041
36,2500	0,000	0,031	0,969	0,969	-0,031	
47,5000	0,000	0,021	0,979	0,979	-0,021	
56,0000	0,000	0,000	1,000	1,000	0,000	
Overall FoxP3+ TIL	-1,0000	1,000	1,000	0,000	1,000	0,000
	0,1250	0,933	0,979	0,021	0,954	-0,046
	0,3750	0,900	0,928	0,072	0,972	-0,028
	0,6250	0,700	0,732	0,268	0,968	-0,032
	0,8750	0,667	0,629	0,371	1,038	0,038
	1,1250	0,600	0,546	0,454	1,054	0,054
	1,3750	0,500	0,505	0,495	0,995	-0,005
	1,6250	0,433	0,495	0,505	0,938	-0,062
	1,8750	0,433	0,464	0,536	0,969	-0,031
	2,2500	0,367	0,381	0,619	0,985	-0,015
	2,7500	0,333	0,330	0,670	1,003	0,003
	3,2500	0,267	0,237	0,763	1,030	0,030
	3,7500	0,267	0,196	0,804	1,071	0,071
	4,2500	0,200	0,155	0,845	1,045	0,045
	4,7500	0,200	0,134	0,866	1,066	0,066
	5,5000	0,133	0,082	0,918	1,051	0,051
	6,2500	0,100	0,062	0,938	1,038	0,038
	6,7500	0,067	0,062	0,938	1,005	0,005
	7,2500	0,067	0,052	0,948	1,015	0,015
	8,0000	0,033	0,052	0,948	0,982	-0,018
9,2500	0,033	0,031	0,969	1,002	0,002	
11,2500	0,000	0,031	0,969	0,969	-0,031	
13,7500	0,000	0,021	0,979	0,979	-0,021	
20,0000	0,000	0,010	0,990	0,990	-0,010	
26,0000	0,000	0,000	1,000	1,000	0,000	
stromal CD3+ TIL	-0,5000	1,000	1,000	0,000	1,000	0,000
	0,6250	0,971	0,944	0,056	1,026	0,026
	0,8750	0,941	0,944	0,056	0,997	-0,003

	1,1250	0,941	0,935	0,065	1,006	0,006
	1,3750	0,941	0,926	0,074	1,015	0,015
	2,1250	0,941	0,917	0,083	1,025	0,025
	2,8750	0,941	0,889	0,111	1,052	0,052
	3,5000	0,912	0,880	0,120	1,032	0,032
	4,2500	0,912	0,861	0,139	1,051	0,051
	4,7500	0,912	0,852	0,148	1,060	0,060
	5,1250	0,853	0,833	0,167	1,020	0,020
	5,6250	0,853	0,824	0,176	1,029	0,029
	6,2500	0,853	0,815	0,185	1,038	0,038
	6,7500	0,824	0,815	0,185	1,009	0,009
	7,2500	0,794	0,778	0,222	1,016	0,016
	8,0000	0,794	0,769	0,231	1,026	0,026
	8,7500	0,794	0,741	0,259	1,053	0,053
	9,5000	0,765	0,741	0,259	1,024	0,024
	10,7500	0,706	0,731	0,269	0,974	-0,026
	12,0000	0,706	0,722	0,278	0,984	-0,016
	13,7500	0,706	0,685	0,315	1,021	0,021
	15,1250	0,706	0,667	0,333	1,039	0,039
	15,6250	0,706	0,657	0,343	1,048	0,048
	16,7500	0,706	0,648	0,352	1,058	0,058
	18,7500	0,706	0,630	0,370	1,076	0,076
	20,5000	0,706	0,602	0,398	1,104	0,104
	21,2500	0,706	0,593	0,407	1,113	0,113
	22,0000	0,706	0,574	0,426	1,132	0,132
	23,0000	0,647	0,556	0,444	1,092	0,092
	24,2500	0,647	0,537	0,463	1,110	0,110
	25,1250	0,647	0,528	0,472	1,119	0,119
	25,3750	0,588	0,519	0,481	1,070	0,070
	26,0000	0,588	0,509	0,491	1,079	0,079
	27,0000	0,588	0,500	0,500	1,088	0,088
	28,0000	0,588	0,472	0,528	1,116	0,116
	29,2500	0,559	0,472	0,528	1,087	0,087
	32,5000	0,441	0,463	0,537	0,978	-0,022
	36,2500	0,412	0,435	0,565	0,977	-0,023
	38,0000	0,382	0,417	0,583	0,966	-0,034
	39,2500	0,382	0,407	0,593	0,975	-0,025
	41,2500	0,324	0,343	0,657	0,981	-0,019
	43,7500	0,324	0,333	0,667	0,990	-0,010
	46,2500	0,265	0,315	0,685	0,950	-0,050
	48,7500	0,265	0,296	0,704	0,968	-0,032
	52,5000	0,206	0,222	0,778	0,984	-0,016
	56,2500	0,176	0,213	0,787	0,964	-0,036
	58,7500	0,176	0,204	0,796	0,973	-0,027
	62,5000	0,118	0,167	0,833	0,951	-0,049
	67,5000	0,118	0,130	0,870	0,988	-0,012
	72,5000	0,088	0,102	0,898	0,986	-0,014
	77,5000	0,029	0,074	0,926	0,955	-0,045
	83,7500	0,000	0,028	0,972	0,972	-0,028
	88,7500	0,000	0,019	0,981	0,981	-0,019
	92,5000	0,000	0,009	0,991	0,991	-0,009
	96,0000	0,000	0,000	1,000	1,000	0,000
epithelial CD3+ TIL	-0,5000	1,000	1,000	0,000	1,000	0,000
	0,7500	0,971	0,981	0,019	0,989	-0,011
	1,2500	0,912	0,870	0,130	1,041	0,041
	1,7500	0,882	0,759	0,241	1,123	0,123
	2,2500	0,765	0,667	0,333	1,098	0,098
	2,7500	0,676	0,620	0,380	1,056	0,056
	3,2500	0,618	0,556	0,444	1,062	0,062
	3,7500	0,588	0,546	0,454	1,042	0,042
	4,2500	0,500	0,500	0,500	1,000	0,000
	4,7500	0,500	0,481	0,519	1,019	0,019
	5,2500	0,500	0,426	0,574	1,074	0,074
	5,7500	0,471	0,407	0,593	1,063	0,063
	6,2500	0,441	0,352	0,648	1,089	0,089
	6,7500	0,441	0,343	0,657	1,099	0,099
	7,2500	0,382	0,315	0,685	1,068	0,068
	7,7500	0,353	0,278	0,722	1,075	0,075
	8,2500	0,353	0,241	0,759	1,112	0,112
	8,7500	0,294	0,222	0,778	1,072	0,072
	9,5000	0,176	0,222	0,778	0,954	-0,046
	10,2500	0,118	0,185	0,815	0,932	-0,068
	10,7500	0,118	0,176	0,824	0,942	-0,058
	11,5000	0,088	0,148	0,852	0,940	-0,060
	12,5000	0,059	0,139	0,861	0,920	-0,080
	13,5000	0,059	0,130	0,870	0,929	-0,071
	14,2500	0,059	0,102	0,898	0,957	-0,043
	15,2500	0,059	0,093	0,907	0,966	-0,034
	16,7500	0,029	0,093	0,907	0,937	-0,063
	19,0000	0,029	0,065	0,935	0,965	-0,035
	21,2500	0,029	0,056	0,944	0,974	-0,026
	22,7500	0,029	0,046	0,954	0,983	-0,017
	24,0000	0,029	0,037	0,963	0,992	-0,008
	24,7500	0,029	0,028	0,972	1,002	0,002
	30,5000	0,000	0,019	0,981	0,981	-0,019
	47,7500	0,000	0,009	0,991	0,991	-0,009
	60,5000	0,000	0,000	1,000	1,000	0,000
stromal CD8+ TIL	-1,0000	1,000	1,000	0,000	1,000	0,000
	0,1250	0,971	0,972	0,028	0,998	-0,002
	0,3750	0,971	0,954	0,046	1,017	0,017
	0,6250	0,912	0,880	0,120	1,032	0,032
	0,8750	0,912	0,861	0,139	1,051	0,051
	1,1250	0,882	0,843	0,157	1,040	0,040
	1,3750	0,853	0,824	0,176	1,029	0,029
	1,6250	0,853	0,815	0,185	1,038	0,038
	1,8750	0,853	0,806	0,194	1,047	0,047
	2,2500	0,853	0,713	0,287	1,140	0,140
	2,7500	0,853	0,685	0,315	1,168	0,168
	3,5000	0,735	0,620	0,380	1,115	0,115
	4,5000	0,706	0,593	0,407	1,113	0,113
	5,1250	0,618	0,556	0,444	1,062	0,062
	5,6250	0,618	0,546	0,454	1,071	0,071
	6,2500	0,618	0,537	0,463	1,081	0,081
	6,7500	0,588	0,509	0,491	1,079	0,079
	7,2500	0,588	0,491	0,509	1,097	0,097
	7,6250	0,559	0,472	0,528	1,087	0,087
	7,8750	0,559	0,463	0,537	1,096	0,096
	8,5000	0,559	0,454	0,546	1,105	0,105
	9,5000	0,559	0,435	0,565	1,124	0,124
	10,1250	0,529	0,407	0,593	1,122	0,122
	10,8750	0,500	0,398	0,602	1,102	0,102
	12,0000	0,471	0,398	0,602	1,072	0,072

	13,0000	0,471	0,389	0,611	1,082	0,082
	14,2500	0,412	0,380	0,620	1,032	0,032
	15,1250	0,353	0,370	0,630	0,983	-0,017
	15,8750	0,353	0,361	0,639	0,992	-0,008
	17,0000	0,324	0,361	0,639	0,962	-0,038
	18,7500	0,294	0,343	0,657	0,952	-0,048
	20,7500	0,235	0,324	0,676	0,911	-0,089
	22,0000	0,235	0,315	0,685	0,920	-0,080
	23,0000	0,235	0,306	0,694	0,930	-0,070
	24,2500	0,235	0,296	0,704	0,939	-0,061
	27,5000	0,206	0,241	0,759	0,965	-0,035
	31,7500	0,176	0,231	0,769	0,945	-0,055
	34,2500	0,176	0,222	0,778	0,954	-0,046
	37,5000	0,176	0,148	0,852	1,028	0,028
	41,2500	0,118	0,102	0,898	1,016	0,016
	43,7500	0,118	0,093	0,907	1,025	0,025
	47,5000	0,088	0,093	0,907	0,996	-0,004
	52,5000	0,029	0,056	0,944	0,974	-0,026
	57,5000	0,000	0,046	0,954	0,954	-0,046
	62,5000	0,000	0,037	0,963	0,963	-0,037
	70,0000	0,000	0,019	0,981	0,981	-0,019
	76,0000	0,000	0,000	1,000	1,000	0,000
epithelial CD8+ TIL	-1,0000	1,000	1,000	0,000	1,000	0,000
	0,2500	0,941	0,954	0,046	0,987	-0,013
	0,7500	0,882	0,917	0,083	0,966	-0,034
	1,2500	0,735	0,806	0,194	0,930	-0,070
	1,7500	0,676	0,704	0,296	0,973	-0,027
	2,2500	0,676	0,639	0,361	1,038	0,038
	2,7500	0,647	0,602	0,398	1,045	0,045
	3,2500	0,500	0,546	0,454	0,954	-0,046
	3,7500	0,441	0,519	0,481	0,923	-0,077
	4,2500	0,441	0,435	0,565	1,006	0,006
	4,7500	0,324	0,398	0,602	0,925	-0,075
	5,2500	0,294	0,343	0,657	0,952	-0,048
	5,7500	0,294	0,324	0,676	0,970	-0,030
	6,2500	0,235	0,287	0,713	0,948	-0,052
	6,7500	0,206	0,269	0,731	0,937	-0,063
	7,2500	0,176	0,250	0,750	0,926	-0,074
	7,7500	0,176	0,231	0,769	0,945	-0,055
	8,2500	0,176	0,213	0,787	0,964	-0,036
	8,7500	0,147	0,194	0,806	0,953	-0,047
	9,5000	0,147	0,185	0,815	0,962	-0,038
	10,2500	0,147	0,157	0,843	0,990	-0,010
	10,7500	0,118	0,157	0,843	0,960	-0,040
	11,5000	0,088	0,148	0,852	0,940	-0,060
	12,2500	0,059	0,130	0,870	0,929	-0,071
	12,7500	0,059	0,120	0,880	0,938	-0,062
	13,2500	0,059	0,111	0,889	0,948	-0,052
	13,7500	0,059	0,102	0,898	0,957	-0,043
	14,2500	0,059	0,093	0,907	0,966	-0,034
	14,7500	0,059	0,083	0,917	0,975	-0,025
	15,7500	0,029	0,074	0,926	0,955	-0,045
	16,7500	0,029	0,065	0,935	0,965	-0,035
	17,5000	0,029	0,056	0,944	0,974	-0,026
	19,7500	0,029	0,046	0,954	0,983	-0,017
	21,7500	0,029	0,037	0,963	0,992	-0,008
	22,2500	0,029	0,028	0,972	1,002	0,002
	23,0000	0,029	0,019	0,981	1,011	0,011
	24,2500	0,029	0,009	0,991	1,020	0,020
	25,5000	0,000	0,009	0,991	0,991	-0,009
	27,0000	0,000	0,000	1,000	1,000	0,000
stromal FoxP3+ TIL	-1,0000	1,000	1,000	0,000	1,000	0,000
	0,1250	0,882	0,953	0,047	0,929	-0,071
	0,3750	0,853	0,925	0,075	0,928	-0,072
	0,6250	0,794	0,804	0,196	0,990	-0,010
	0,8750	0,765	0,776	0,224	0,989	-0,011
	1,1250	0,735	0,738	0,262	0,997	-0,003
	1,3750	0,676	0,673	0,327	1,004	0,004
	1,6250	0,676	0,636	0,364	1,041	0,041
	1,8750	0,647	0,617	0,383	1,030	0,030
	2,2500	0,559	0,561	0,439	0,998	-0,002
	2,6250	0,529	0,533	0,467	0,997	-0,003
	2,8750	0,529	0,514	0,486	1,015	0,015
	3,2500	0,441	0,486	0,514	0,955	-0,045
	3,6250	0,412	0,477	0,523	0,935	-0,065
	3,8750	0,412	0,467	0,533	0,944	-0,056
	4,5000	0,382	0,411	0,589	0,971	-0,029
	5,5000	0,324	0,299	0,701	1,024	0,024
	6,5000	0,324	0,252	0,748	1,071	0,071
	7,2500	0,324	0,215	0,785	1,109	0,109
	8,0000	0,324	0,168	0,832	1,155	0,155
	8,7500	0,265	0,159	0,841	1,106	0,106
	9,5000	0,265	0,150	0,850	1,115	0,115
	10,5000	0,206	0,121	0,879	1,084	0,084
	11,7500	0,206	0,103	0,897	1,103	0,103
	13,0000	0,147	0,093	0,907	1,054	0,054
	14,2500	0,147	0,084	0,916	1,063	0,063
	15,1250	0,118	0,047	0,953	1,071	0,071
	16,3750	0,118	0,037	0,963	1,080	0,080
	18,0000	0,088	0,037	0,963	1,051	0,051
	19,2500	0,088	0,028	0,972	1,060	0,060
	22,6250	0,029	0,019	0,981	1,011	0,011
	27,6250	0,029	0,009	0,991	1,020	0,020
	32,5000	0,000	0,009	0,991	0,991	-0,009
	36,0000	0,000	0,000	1,000	1,000	0,000
epithelial FoxP3+ TIL	-1,0000	1,000	1,000	0,000	1,000	0,000
	0,2500	0,853	0,860	0,140	0,993	-0,007
	0,7500	0,706	0,766	0,234	0,940	-0,060
	1,2500	0,382	0,439	0,561	0,943	-0,057
	1,7500	0,235	0,252	0,748	0,983	-0,017
	2,2500	0,147	0,159	0,841	0,988	-0,012
	2,7500	0,118	0,075	0,925	1,043	0,043
	3,2500	0,088	0,056	0,944	1,032	0,032
	3,7500	0,088	0,037	0,963	1,051	0,051
	5,0000	0,088	0,019	0,981	1,070	0,070
	6,2500	0,059	0,000	1,000	1,059	0,059
	7,5000	0,029	0,000	1,000	1,029	0,029
	9,5000	0,000	0,000	1,000	1,000	0,000

Supplementary Table 1: Calculation of Youden index by ROC analysis

Exon 9		Exon 11		Exon 14	
c.853T>C	p.F285L	c.1102G>T	p.D368Y	c.1388C>A	p.A463D
c.857C>G	p.P286R			c.1388C>A	p.A463D
c.857C>G	p.P286R				
c.857C>G	p.P286R				
c.857C>G	p.P286R				

Supplementary Table 2: List of POLE mutations

	Infiltration density / absolute values			
	Mean	Median	Minimum	Maximum
overall T-cells (CD3+; % of tumor area)	10.78	6.00	0.00	70.00
epithelial T-cells (CD3+; tumor epithelium; punctum maximum)	6.62	4.28	0.00	60.00
stromal T-cells (CD3+; % of intratumoral stroma)	32.93	28.00	0.00	95.00
overall T-Killer cells (CD8+; % of tumor area)	7.45	3.25	0.00	55.00
epithelial T-Killer cells (CD8+; tumor epithelium; punctum maximum)	5.38	3.75	0.00	26.00
stromal T-Killer cells (CD8+; % of intratumoral stroma)	16.22	7.50	0.00	75.00
overall regulatory T-cells (FoxP3+% of tumor area)	2.38	1.25	0.00	25.00
epithelial regulatory T-cells (FoxP3+; tumor epithelium; punctum maximum)	1.40	1.00	0.00	9.00
stromal regulatory T-cells (FoxP3+; % of intratumoral stroma)	5.14	3.00	0.00	35.00

Supplementary Table 3: Absolute values (mean; median; range) of infiltration densities of tumor infiltrating lymphocytes

		Grading (WHO)						Grading (WHO)						p53 status		Microsatellite status						Microsatellite status						POLE status							
		G1		G2		G3		low grade (G1/G2)		high grade (G3)		mutated		wildtype		MSI		MSS		MLH1/MSH2 loss		MSH2/MSH6 loss		MSS		wildtype		mutated							
		n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%						
stromal TIL (CD3)	low	23	16.20%	26	18.30%	14	9.90%	0.005	49	34.50%	14	9.90%	0.001	9	6.30%	54	38.00%	0.951	13	9.20%	50	35.20%	0.002	50	35.20%	10	7.00%	3	2.10%	0.005	62	43.70%	1	0.70%	0.100
	high	22	15.50%	19	13.40%	38	26.80%		41	29.90%	38	26.80%		11	7.70%	68	47.90%		36	25.40%	43	30.30%		43	30.30%	32	22.50%	4	2.80%		73	51.40%	6	4.20%	
epithelial TIL (CD3)	low	11	7.70%	15	10.60%	4	2.80%	0.007	26	18.30%	4	2.80%	0.003	1	0.70%	29	20.40%	0.057	5	3.50%	25	17.60%	0.021	25	17.60%	4	2.80%	1	0.70%	0.066	30	21.10%	0	0.00%	0.160
	high	34	23.90%	30	21.10%	48	33.80%		64	45.10%	48	33.80%		19	13.40%	93	65.50%		64	45.10%	68	47.90%		68	47.90%	38	26.80%	6	4.20%		105	73.90%	7	4.90%	
stromal T-Killer cells (CD8)	low	18	12.70%	18	12.70%	3	2.10%	<0.001	36	25.40%	3	2.10%	<0.001	6	4.20%	33	23.20%	0.784	10	7.00%	29	20.40%	0.171	29	20.40%	6	4.20%	4	2.80%	0.025	37	26.10%	2	1.40%	0.846
	high	27	19.00%	27	19.00%	49	34.50%		54	38.00%	49	34.50%		14	9.90%	89	62.70%		39	27.50%	64	45.10%		64	45.10%	36	25.40%	3	2.10%		98	69.00%	5	3.50%	
epithelial T-Killer cells (CD8)	low	23	16.20%	32	22.50%	16	11.30%	<0.001	55	38.70%	16	11.30%	<0.001	11	7.70%	60	42.30%	0.629	20	14.10%	51	35.90%	0.112	51	35.90%	15	10.60%	5	3.50%	0.061	70	49.30%	1	0.70%	0.053
	high	22	15.50%	13	9.20%	36	25.40%		35	24.60%	36	25.40%		9	6.30%	62	43.70%		29	20.40%	42	29.60%		42	29.60%	27	19.00%	2	1.40%		65	45.80%	6	4.20%	
stromal regulatory T-cells (FoxP3)	low	43	30.30%	38	26.80%	32	22.50%	<0.001	81	57.00%	32	22.50%	<0.001	19	13.40%	94	66.20%	0.065	36	25.40%	77	54.20%	0.190	77	54.20%	29	20.40%	7	4.90%	0.072	108	76.10%	5	3.50%	0.583
	high	2	1.40%	7	4.90%	20	14.10%		9	6.30%	20	14.10%		1	0.70%	28	19.70%		13	9.20%	16	11.30%		16	11.30%	13	9.20%	0	0.00%		27	19.00%	2	1.40%	
epithelial regulatory T-cells (FoxP3)	low	45	31.70%	44	31.00%	48	33.80%	0.104	89	62.70%	48	33.80%	0.004	20	14.10%	117	82.40%	0.357	47	33.10%	90	63.40%	0.793	90	63.40%	40	28.20%	7	4.90%	0.791	131	92.30%	6	4.20%	0.113
	high	0	0.00%	1	0.70%	4	2.80%		1	0.70%	4	2.80%		0	0.00%	5	3.50%		2	1.40%	3	2.10%		3	2.10%	2	1.40%	0	0.00%		4	2.80%	1	0.70%	

Supplementary Table 4: Correlation of immunologic variables (intraepithelial TIL) with morphomolecular data

		Age		T Stage												N Stage												M Stage												FIGO Stage												FIGO Stage											
		median and below	above median	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%																				
overall TIL (CD3)	low	47	31.0%	44	31.0%	0.764	68	47.9%	13	9.2%	9	6.3%	1	0.7%	0.480	87	61.3%	4	2.8%	0.100	88	62.0%	3	2.1%	0.230	67	47.2%	12	8.5%	9	6.3%	3	2.1%	0.537	79	55.6%	12	8.5%	0.192																								
stromal TIL (CD3)	low	25	17.6%	26	18.3%	0.888	33	23.2%	11	7.7%	7	4.9%	0	0.0%	0.000	45	31.7%	6	4.2%	0.773	47	33.1%	4	2.8%	0.934	33	23.2%	7	4.9%	7	4.9%	4	2.8%	0.941	40	28.2%	11	7.7%	0.581																								
epithelial TIL (CD3)	low	17	26.1%	26	18.3%	0.746	46	32.4%	10	7.0%	7	4.9%	0	0.0%	0.865	59	41.5%	4	2.8%	0.090	60	42.3%	3	2.1%	0.649	45	31.7%	9	6.3%	6	4.2%	3	2.1%	0.666	54	38.0%	9	6.3%	0.632																								
overall T-Killer cells (CD8)	low	35	24.4%	26	18.3%	0.168	48	33.8%	18	12.7%	1	0.7%	0	0.0%	0.332	59	41.5%	2	1.4%	0.128	59	41.5%	2	1.4%	0.430	48	33.8%	7	4.9%	4	2.8%	2	1.4%	0.259	55	38.7%	6	4.2%	0.074																								
stromal T-Killer cells (CD8)	low	17	26.1%	44	31.0%	0.019	53	37.3%	16	11.3%	1	0.7%	0	0.0%	0.167	73	51.4%	8	5.6%	0.044	76	53.5%	5	3.5%	0.423	52	36.6%	12	8.5%	12	8.5%	5	3.5%	0.155	64	45.1%	12	8.5%	0.091																								
epithelial T-Killer cells (CD8)	low	26	18.3%	13	9.2%	0.737	48	33.8%	13	9.2%	9	6.3%	1	0.7%	0.645	39	27.5%	0	0.0%	0.512	38	26.8%	1	0.7%	0.698	33	23.2%	3	2.1%	2	1.4%	1	0.7%	0.655	36	25.4%	3	2.1%	0.820																								
overall regulatory T-cells (FoxP3)	low	46	32.4%	57	40.1%	0.447	68	47.9%	21	14.8%	13	9.2%	1	0.7%	0.185	93	65.5%	10	7.0%	0.095	97	68.3%	6	4.2%	0.115	67	47.2%	16	11.3%	14	9.9%	6	4.2%	0.203	83	58.5%	20	14.1%	0.047																								
stromal regulatory T-cells (FoxP3)	low	16	11.3%	12	8.5%	0.590	16	11.3%	6	4.2%	6	4.2%	0	0.0%	0.000	24	16.9%	4	2.8%	0.973	25	17.6%	3	2.1%	0.023	16	11.3%	4	2.8%	5	3.5%	3	2.1%	0.066	20	14.1%	8	5.6%	0.462																								
epithelial regulatory T-cells (FoxP3)	low	56	39.4%	57	40.1%	0.626	83	58.5%	18	12.7%	11	7.7%	1	0.7%	0.544	105	73.9%	8	5.6%	0.000	110	77.5%	3	2.1%	0.023	82	57.7%	14	9.9%	14	9.9%	3	2.1%	0.066	96	67.6%	17	12.0%	0.814																								
	high	16	11.3%	13	9.2%		18	12.7%	6	4.2%	5	3.5%	0	0.0%		27	19.0%	2	1.4%		25	17.6%	4	2.8%		18	12.7%	5	3.5%	2	1.4%	4	2.8%		23	16.2%	6	4.2%																									
	low	70	49.3%	67	47.2%	0.626	98	69.0%	23	16.2%	15	10.6%	1	0.7%	0.917	127	89.4%	10	7.0%	0.532	130	91.5%	7	4.9%	0.604	97	68.3%	18	12.7%	15	10.6%	7	4.9%	0.836	115	81.0%	22	15.5%	0.814																								
	high	2	1.4%	3	2.1%		3	2.1%	1	0.7%	1	0.7%	0	0.0%		5	3.5%	0	0.0%		5	3.5%	0	0.0%		3	2.1%	1	0.7%	1	0.7%	0	0.0%	4	2.8%	1	0.7%																										

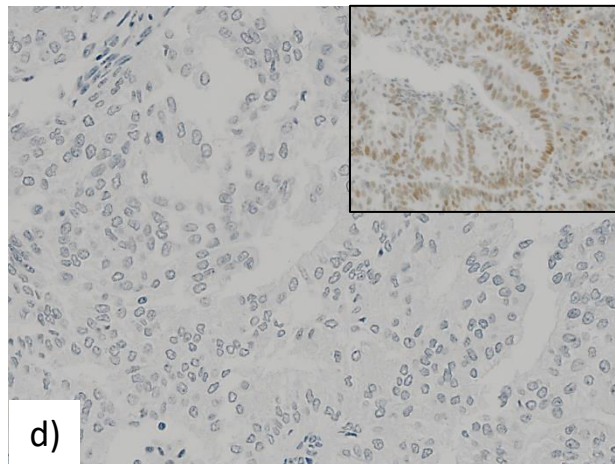
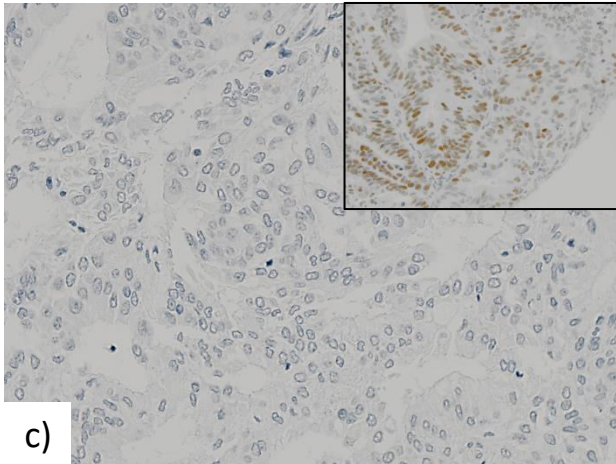
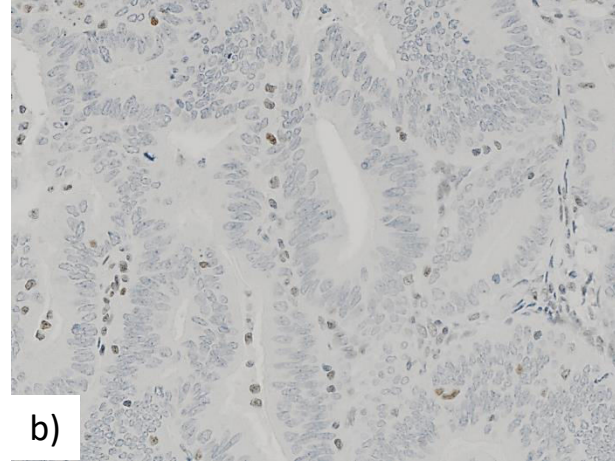
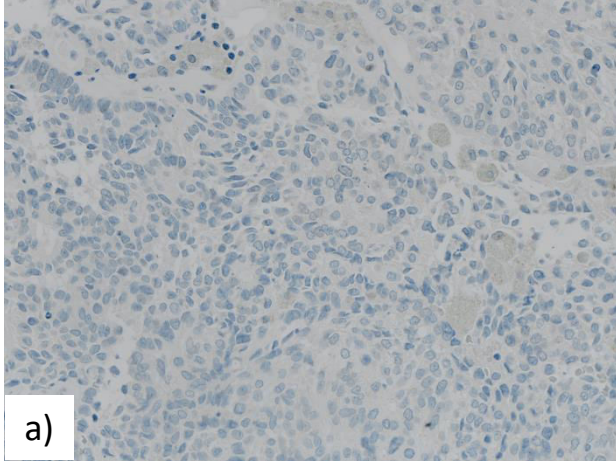
Supplementary Table S1: Correlation of immunologic with clinical data

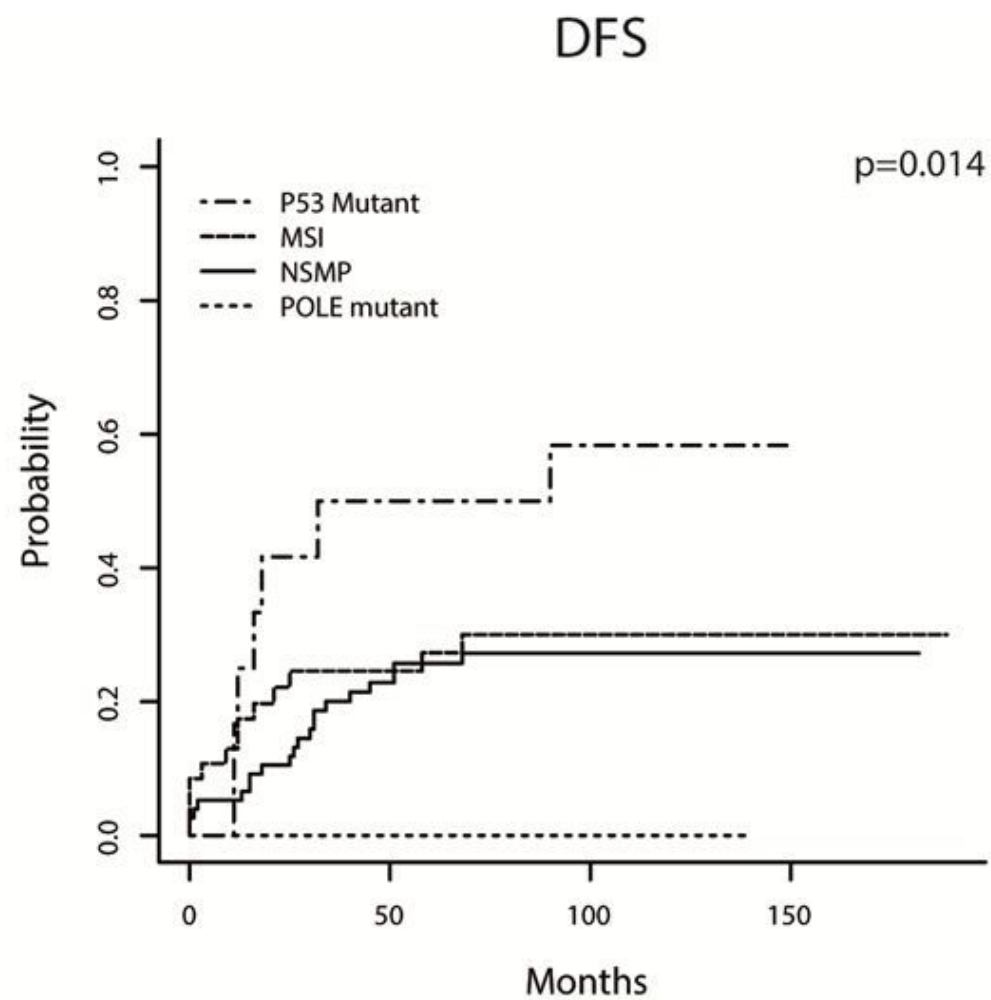
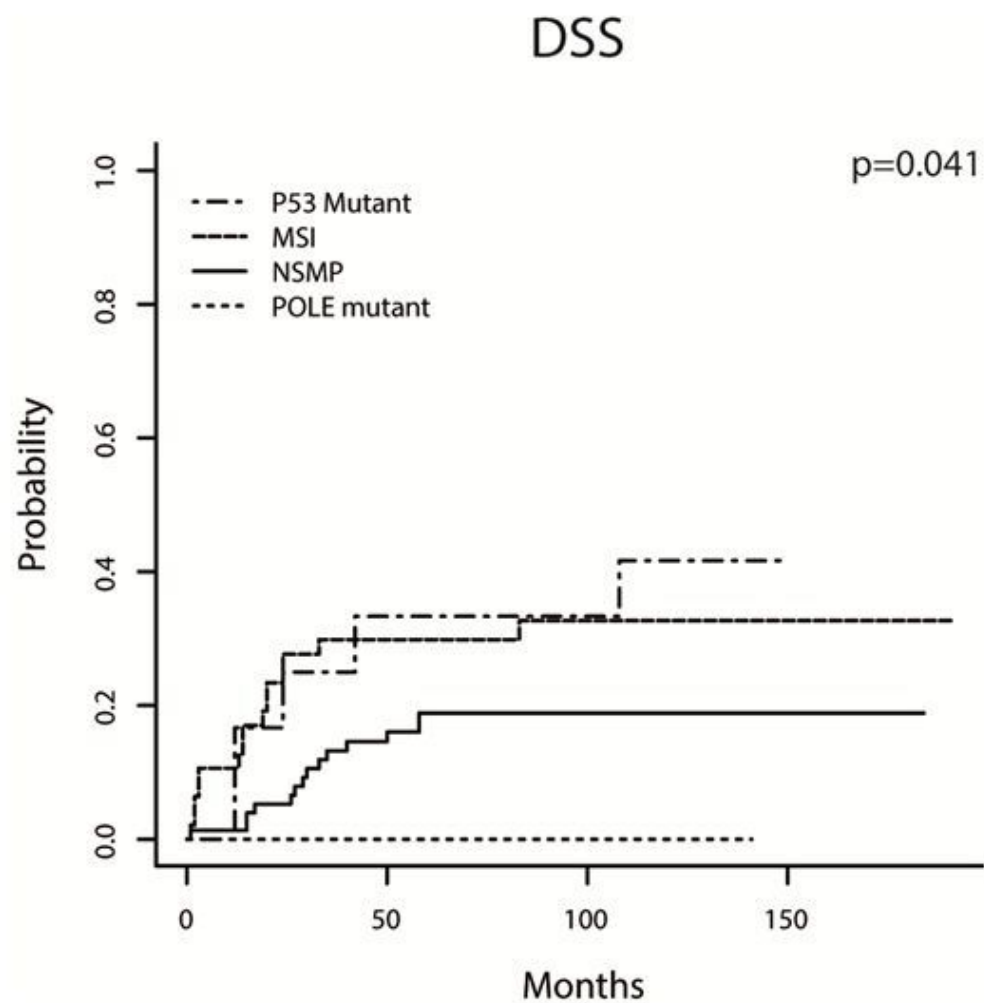
		Grading (WHO)						p-value	Grading (WHO)				p-value	p53 status				p-value
		1		2		3			low-grade		high-grade			mutated		wildtype		
		n	%	n	%	n	%		n	%	n	%		n	%	n	%	
overall TIL (CD3)	low	30	34,10%	23	26,10%	11	12,50%	<0,001	53	60,20%	11	12,50%	<0,001	9	10,20%	55	62,50%	0,849
	high	3	3,40%	6	6,80%	15	17,00%		9	10,20%	15	17,00%		3	3,40%	21	23,90%	
stromal TIL (CD3)	low	21	23,90%	18	20,50%	10	11,40%	0,108	39	44,30%	10	11,40%	0,035	5	5,70%	44	50,00%	0,293
	high	12	13,60%	11	12,50%	16	18,20%		23	26,10%	16	18,20%		7	8,00%	32	36,40%	
epithelial TIL (CD3)	low	10	11,40%	11	12,50%	4	4,50%	0,172	21	23,90%	4	4,50%	0,079	0	0,00%	25	28,40%	0,019
	high	23	26,10%	18	20,50%	22	25,00%		41	46,60%	22	25,00%		12	13,60%	51	58,00%	
overall T-Killer cells (CD8)	low	23	26,10%	16	18,20%	5	5,70%	<0,001	39	44,30%	5	5,70%	<0,001	6	6,80%	38	43,20%	1,000
	high	10	11,40%	13	14,80%	21	23,90%		23	26,10%	21	23,90%		6	6,80%	38	43,20%	
stromal T-Killer cells (CD8)	low	13	14,80%	13	14,80%	2	2,30%	0,006	26	29,50%	2	2,30%	0,002	3	3,40%	25	28,40%	0,585
	high	20	22,70%	16	18,20%	24	27,30%		36	40,90%	24	27,30%		9	10,20%	51	58,00%	
epithelial T-Killer cells (CD8)	low	16	18,20%	22	25,00%	12	13,60%	0,04	38	43,20%	12	13,60%	0,191	7	8,00%	43	48,90%	0,909
	high	17	19,30%	7	8,00%	14	15,90%		24	27,30%	14	15,90%		5	5,70%	33	37,50%	
overall regulatory T-cells (FoxP3)	low	33	37,50%	24	27,30%	19	21,60%	0,009	57	64,80%	19	21,60%	0,019	11	12,50%	65	73,90%	0,565
	high	0	0,00%	5	5,70%	7	8,00%		5	5,70%	7	8,00%		1	1,10%	11	12,50%	
stromal regulatory T-cells (FoxP3)	low	31	35,20%	24	27,30%	18	20,50%	0,043	55	62,50%	18	20,50%	0,027	11	12,50%	62	70,50%	0,388
	high	2	2,30%	5	5,70%	8	9,10%		7	8,00%	8	9,10%		1	1,10%	14	15,90%	
epithelial regulatory T-cells (FoxP3)	low	33	37,50%	28	31,80%	24	27,30%	0,271	61	69,30%	24	27,30%	0,152	12	13,60%	73	83,00%	0,484
	high	0	0,00%	1	1,10%	2	2,30%		1	1,10%	2	2,30%		0	0,00%	3	3,40%	

Supplementary Table 6: Correlation of immunologic data with morphomolecular data in the subgroup of POLE wildtype and microsatellite stable (MSS) endometrial carcinomas

		Overall	Events (OS)	Events (DSS)	Events (DFS)
overall TIL (CD3)	low	91	30	18	22
	high	51	24	16	16
stromal TIL (CD3)	low	63	19	12	16
	high	79	35	22	22
epithelial TIL (CD3)	low	30	8	4	8
	high	112	46	30	30
overall T-Killer cells (CD8)	low	61	18	9	11
	high	81	36	25	27
stromal T-Killer cells (CD8)	low	39	9	5	6
	high	103	45	29	32
epithelial T-Killer cells (CD8)	low	71	26	19	23
	high	71	28	15	15
overall regulatory T-cells (FoxP3)	low	114	41	25	27
	high	28	13	9	11
stromal regulatory T-cells (FoxP3)	low	113	40	23	26
	high	29	14	11	12
epithelial regulatory T-cells (FoxP3)	low	137	50	31	26
	high	5	4	3	2

Supplementary Table 7: Contexture of immunologic tumor microenvironment and survival associations





Supplementary Figure 2: Cumulative incidence function visualizing disease-specific and disease-free survival depending on molecular subgroups; a) disease-specific survival; b) disease-free survival.