analysis of imvigor010 in ctDNA +, how OS events accumulate

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prevalence

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## [1] "STRAT1NM : NUMBER OF LYMPH NODES(<10 vs. >=10)"
## [1] "STRAT2NM : NODAL STATUS (postitive vs. negative)"
## [1] "STRAT3NM : TUMOUR STAGE (<=PT2/PT2 vs. PT3/PT4)"
## [1] "STRAT4NM : ACCI"
## [1] "STRAT5NM : PRIOR NEOADJUVANT CHEMOTHERAPY (YES vs. NO)"
## [1] "STRAT6NM : PDL1 STATUS (IC0/1 vs. IC2/3)"
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Table 1: stratification factors in impow010 ctDNA +

var	name	referLevel	targetLevel	freq
STRAT2	NODAL STATUS (postitive vs. negative)	POSITIVE	NEGATIVE	0.33
STRAT3	TUMOUR STAGE (<=PT2/PT2 vs. PT3/PT4)	PT3/PT4	<PT2/PT2	0.21
STRAT6	PDL1 STATUS (IC0/1 vs. IC2/3)	IC 0/1	IC 2/3	0.48

Table 2: freq in 214 ctDNA+ patients

STRAT2	STRAT3	STRAT6	Count	freq
POSITIVE	PT3/PT4	IC 0/1	52	0.243
NEGATIVE	PT3/PT4	IC 0/1	33	0.154
POSITIVE	<PT2/PT2	IC 0/1	23	0.107
NEGATIVE	<PT2/PT2	IC 0/1	4	0.019
POSITIVE	PT3/PT4	IC 2/3	52	0.243
NEGATIVE	PT3/PT4	IC 2/3	31	0.145
POSITIVE	<PT2/PT2	IC 2/3	17	0.079
NEGATIVE	<PT2/PT2	IC 2/3	2	0.009

DFS

[1] “arm= ATEZOLIZUMAB (MPDL3280A) 1200 MG ctDNA= NEGATIVE” Call: coxph(formula = Surv(AVAL, event) ~ STRAT2, data = d)

```
               coef exp(coef) se(coef)      z       p
```

STRAT2NEGATIVE -0.5687 0.5663 0.2176 -2.613 0.00896

Likelihood ratio test=6.76 on 1 df, p=0.009342 n= 184, number of events= 85

[1] “arm= ATEZOLIZUMAB (MPDL3280A) 1200 MG ctDNA= POSITIVE” Call: coxph(formula = Surv(AVAL, event) ~ STRAT2, data = d)

```
               coef exp(coef) se(coef)      z     p
```

STRAT2NEGATIVE -0.2043 0.8152 0.2288 -0.893 0.372

Likelihood ratio test=0.82 on 1 df, p=0.3653 n= 116, number of events= 96

[1] “arm= OBSERVATION ctDNA= NEGATIVE” Call: coxph(formula = Surv(AVAL, event) ~ STRAT2, data = d)

```
               coef exp(coef) se(coef)      z      p
```

STRAT2NEGATIVE -0.5978 0.5500 0.2423 -2.467 0.0136

Likelihood ratio test=6.17 on 1 df, p=0.01298 n= 183, number of events= 70

[1] “arm= OBSERVATION ctDNA= POSITIVE” Call: coxph(formula = Surv(AVAL, event) ~ STRAT2, data = d)

```
                 coef exp(coef)  se(coef)      z     p
```

STRAT2NEGATIVE -0.003386 0.996619 0.224075 -0.015 0.988

Likelihood ratio test=0 on 1 df, p=0.9879 n= 98, number of events= 87

[1] “arm= ATEZOLIZUMAB (MPDL3280A) 1200 MG ctDNA= NEGATIVE” Call: coxph(formula = Surv(AVAL, event) ~ STRAT3, data = d)

```
               coef exp(coef) se(coef)     z     p
```

STRAT3<PT2/PT2 0.02336 1.02363 0.23542 0.099 0.921

Likelihood ratio test=0.01 on 1 df, p=0.9211 n= 184, number of events= 85

[1] “arm= ATEZOLIZUMAB (MPDL3280A) 1200 MG ctDNA= POSITIVE” Call: coxph(formula = Surv(AVAL, event) ~ STRAT3, data = d)

```
               coef exp(coef) se(coef)      z      p
```

STRAT3<PT2/PT2 -0.6306 0.5323 0.2823 -2.234 0.0255

Likelihood ratio test=5.72 on 1 df, p=0.01679 n= 116, number of events= 96

[1] “arm= OBSERVATION ctDNA= NEGATIVE” Call: coxph(formula = Surv(AVAL, event) ~ STRAT3, data = d)

```
               coef exp(coef) se(coef)      z     p
```

STRAT3<PT2/PT2 -0.4676 0.6265 0.2915 -1.604 0.109

Likelihood ratio test=2.8 on 1 df, p=0.09441 n= 183, number of events= 70

[1] “arm= OBSERVATION ctDNA= POSITIVE” Call: coxph(formula = Surv(AVAL, event) ~ STRAT3, data = d)

```
               coef exp(coef) se(coef)      z       p
```

STRAT3<PT2/PT2 -0.8856 0.4125 0.2853 -3.104 0.00191

Likelihood ratio test=11.26 on 1 df, p=0.0007919 n= 98, number of events= 87

[1] “arm= ATEZOLIZUMAB (MPDL3280A) 1200 MG ctDNA= NEGATIVE” Call: coxph(formula = Surv(AVAL, event) ~ STRAT6, data = d)

```
             coef exp(coef) se(coef)      z       p
```

STRAT6IC 2/3 -0.7700 0.4630 0.2401 -3.207 0.00134

Likelihood ratio test=11.2 on 1 df, p=0.0008198 n= 184, number of events= 85

[1] “arm= ATEZOLIZUMAB (MPDL3280A) 1200 MG ctDNA= POSITIVE” Call: coxph(formula = Surv(AVAL, event) ~ STRAT6, data = d)

```
            coef exp(coef) se(coef)      z      p
```

STRAT6IC 2/3 -0.5057 0.6031 0.2063 -2.452 0.0142

Likelihood ratio test=5.98 on 1 df, p=0.01446 n= 116, number of events= 96

[1] “arm= OBSERVATION ctDNA= NEGATIVE” Call: coxph(formula = Surv(AVAL, event) ~ STRAT6, data = d)

```
            coef exp(coef) se(coef)      z        p
```

STRAT6IC 2/3 -0.9070 0.4038 0.2504 -3.622 0.000292

Likelihood ratio test=13.85 on 1 df, p=0.0001984 n= 183, number of events= 70

[1] “arm= OBSERVATION ctDNA= POSITIVE” Call: coxph(formula = Surv(AVAL, event) ~ STRAT6, data = d)

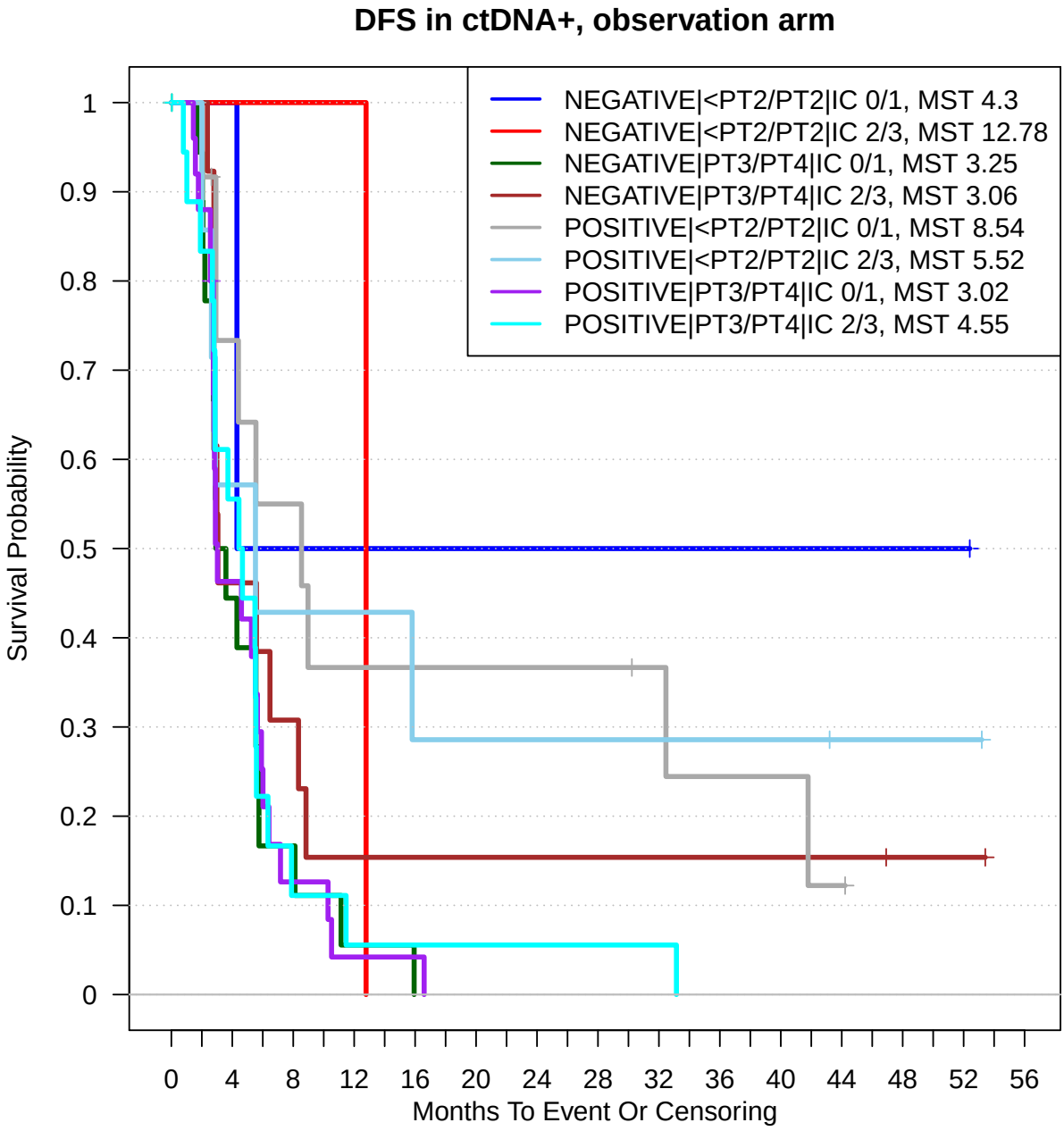
```
            coef exp(coef) se(coef)    z     p
```

STRAT6IC 2/3 -0.1315 0.8768 0.2192 -0.6 0.549

Likelihood ratio test=0.36 on 1 df, p=0.5472 n= 98, number of events= 87

Table 3: prognostic effect for DFS by arm/ctDNA status (# event)

	atezo NEGATIVE	atezo POSITIVE	Obs NEGATIVE	Obs POSITIVE
c_node	-0.57 (85)	-0.2 (96)	-0.6 (70)	0 (87)
c_stage	0.02 (85)	-0.63 (96)	-0.47 (70)	-0.89 (87)
c_pdl1	-0.77 (85)	-0.51 (96)	-0.91 (70)	-0.13 (87)



NEGATIVE|<PT2/PT2|IC 0/1	2	2	2	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	0	0
NEGATIVE|<PT2/PT2|IC 2/3	1	1	1	1	1	1	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
NEGATIVE|PT3/PT4|IC 0/1	19	17	8	3	3	2	1	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
NEGATIVE|PT3/PT4|IC 2/3	13	13	6	5	4	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	1	1	1	0	0
POSITIVE|<PT2/PT2|IC 0/1	12	12	8	6	6	4	4	4	4	4	4	4	4	4	4	4	3	2	2	2	2	1	1	0	0	0	0	0
POSITIVE|<PT2/PT2|IC 2/3	7	7	4	3	3	3	3	3	2	2	2	2	2	2	2	2	2	2	2	2	2	2	1	1	1	1	1	0	0
POSITIVE|PT3/PT4|IC 0/1	25	22	11	6	3	3	1	1	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
POSITIVE|PT3/PT4|IC 2/3	19	15	10	4	2	2	1	1	1	1	1	1	1	1	1	1	0	0	0	0	0	0	0	0	0	0	0	0

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## [1] ""
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OS

[1] “arm= ATEZOLIZUMAB (MPDL3280A) 1200 MG ctDNA= NEGATIVE” Call: coxph(formula = Surv(AVAL, event) ~ STRAT2, data = d)

	coef	exp(coef)	se(coef)	z	p
STRAT2NEGATIVE	-0.3097	0.7337	0.2657	-1.165	0.244

Likelihood ratio test=1.35 on 1 df, p=0.2461 n= 184, number of events= 57

[1] “arm= ATEZOLIZUMAB (MPDL3280A) 1200 MG ctDNA= POSITIVE” Call: coxph(formula = Surv(AVAL, event) ~ STRAT2, data = d)

	coef	exp(coef)	se(coef)	z	p
STRAT2NEGATIVE	-0.1029	0.9022	0.2649	-0.388	0.698

Likelihood ratio test=0.15 on 1 df, p=0.6957 n= 116, number of events= 70

[1] “arm= OBSERVATION ctDNA= NEGATIVE” Call: coxph(formula = Surv(AVAL, event) ~ STRAT2, data = d)

	coef	exp(coef)	se(coef)	z	p
STRAT2NEGATIVE	-0.4606	0.6309	0.3073	-1.499	0.134

Likelihood ratio test=2.27 on 1 df, p=0.1321 n= 183, number of events= 43

[1] “arm= OBSERVATION ctDNA= POSITIVE” Call: coxph(formula = Surv(AVAL, event) ~ STRAT2, data = d)

	coef	exp(coef)	se(coef)	z	p
STRAT2NEGATIVE	-0.2974	0.7428	0.2549	-1.167	0.243

Likelihood ratio test=1.4 on 1 df, p=0.2362 n= 98, number of events= 70

[1] “arm= ATEZOLIZUMAB (MPDL3280A) 1200 MG ctDNA= NEGATIVE” Call: coxph(formula = Surv(AVAL, event) ~ STRAT3, data = d)

	coef	exp(coef)	se(coef)	z	p
STRAT3<PT2/PT2	0.2670	1.3061	0.2776	0.962	0.336

Likelihood ratio test=0.9 on 1 df, p=0.3431 n= 184, number of events= 57

[1] “arm= ATEZOLIZUMAB (MPDL3280A) 1200 MG ctDNA= POSITIVE” Call: coxph(formula = Surv(AVAL, event) ~ STRAT3, data = d)

	coef	exp(coef)	se(coef)	z	p
STRAT3<PT2/PT2	-0.5943	0.5520	0.3290	-1.806	0.0709

Likelihood ratio test=3.72 on 1 df, p=0.05391 n= 116, number of events= 70

[1] “arm= OBSERVATION ctDNA= NEGATIVE” Call: coxph(formula = Surv(AVAL, event) ~ STRAT3, data = d)

	coef	exp(coef)	se(coef)	z	p
STRAT3<PT2/PT2	-0.7630	0.4663	0.4137	-1.845	0.0651

Likelihood ratio test=4 on 1 df, p=0.04553 n= 183, number of events= 43

[1] “arm= OBSERVATION ctDNA= POSITIVE” Call: coxph(formula = Surv(AVAL, event) ~ STRAT3, data = d)

	coef	exp(coef)	se(coef)	z	p

STRAT3<PT2/PT2 -0.7495 0.4726 0.3126 -2.398 0.0165

Likelihood ratio test=6.6 on 1 df, p=0.01018 n= 98, number of events= 70

[1] "arm= ATEZOLIZUMAB (MPDL3280A) 1200 MG ctDNA= NEGATIVE" Call: coxph(formula = Surv(AVAL, event) ~ STRAT6, data = d)

```
            coef exp(coef) se(coef)      z      p
```

STRAT6IC 2/3 -0.6927 0.5002 0.2877 -2.407 0.0161

Likelihood ratio test=6.2 on 1 df, p=0.01275 n= 184, number of events= 57

[1] "arm= ATEZOLIZUMAB (MPDL3280A) 1200 MG ctDNA= POSITIVE" Call: coxph(formula = Surv(AVAL, event) ~ STRAT6, data = d)

```
            coef exp(coef) se(coef)      z       p
```

STRAT6IC 2/3 -0.6447 0.5248 0.2436 -2.646 0.00815

Likelihood ratio test=7.08 on 1 df, p=0.007806 n= 116, number of events= 70

[1] "arm= OBSERVATION ctDNA= NEGATIVE" Call: coxph(formula = Surv(AVAL, event) ~ STRAT6, data = d)

```
            coef exp(coef) se(coef)      z        p
```

STRAT6IC 2/3 -1.1233 0.3252 0.3325 -3.379 0.000729

Likelihood ratio test=12.63 on 1 df, p=0.0003789 n= 183, number of events= 43

[1] "arm= OBSERVATION ctDNA= POSITIVE" Call: coxph(formula = Surv(AVAL, event) ~ STRAT6, data = d)

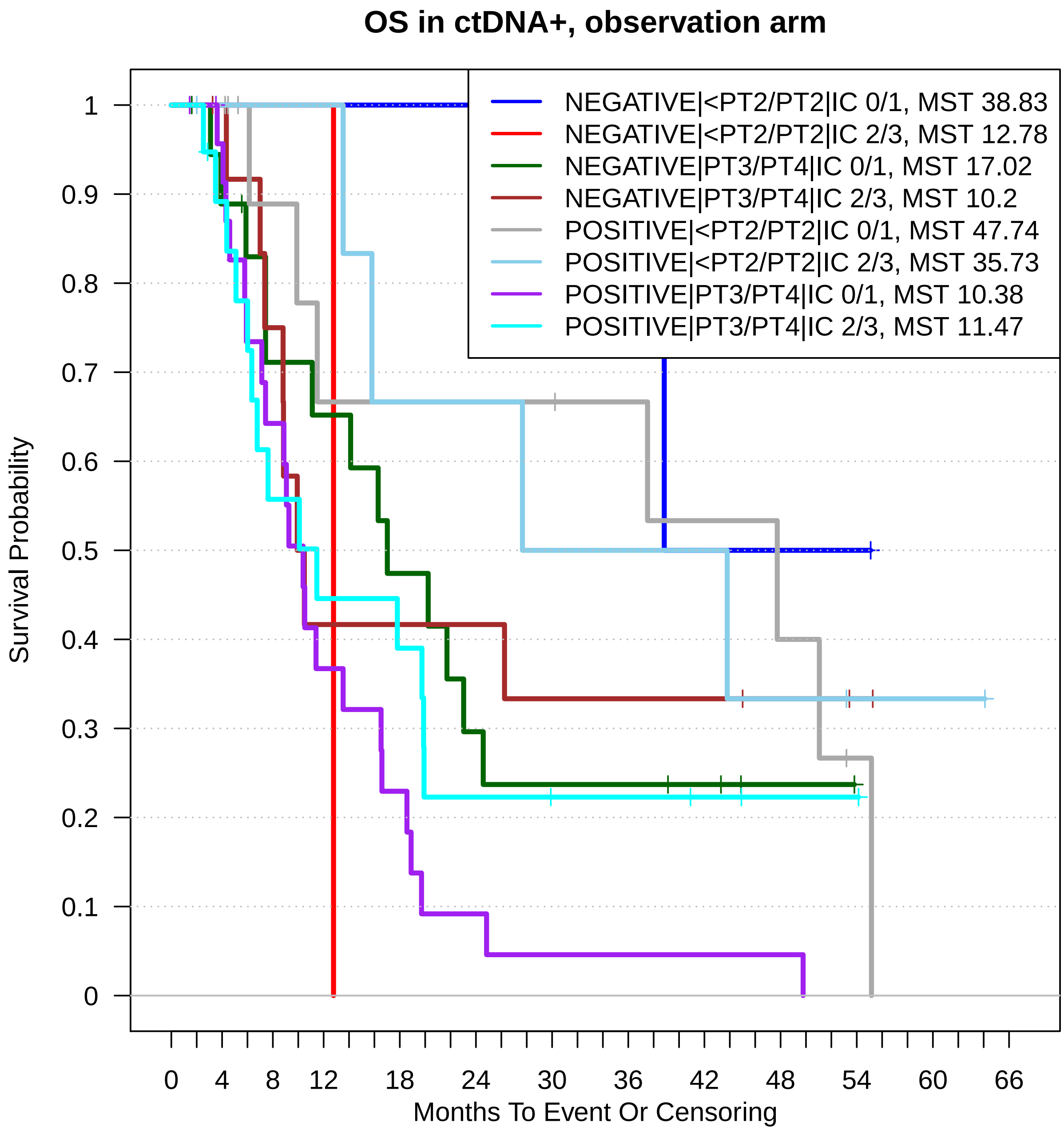
```
            coef exp(coef) se(coef)      z     p
```

STRAT6IC 2/3 -0.1983 0.8201 0.2463 -0.805 0.421

Likelihood ratio test=0.66 on 1 df, p=0.4177 n= 98, number of events= 70

Table 4: prognostic effect for OS by arm/ctDNA status (# event)

	atezo NEGATIVE	atezo POSITIVE	Obs NEGATIVE	Obs POSITIVE
c_node	-0.31 (57)	-0.1 (70)	-0.46 (43)	-0.3 (70)
c_stage	0.27 (57)	-0.59 (70)	-0.76 (43)	-0.75 (70)
c_pdl1	-0.69 (57)	-0.64 (70)	-1.12 (43)	-0.2 (70)



NEGATIVE|<PT2/PT2|IC 0/1	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	1	1	1	1	1	1	1	1	0	0	0	0	0	0
NEGATIVE|<PT2/PT2|IC 2/3	1	1	1	1	1	1	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
NEGATIVE|PT3/PT4|IC 0/1	19	18	16	14	12	12	11	11	10	8	8	6	5	4	4	4	4	4	4	4	3	3	2	1	1	1	1	0	0	0	0	0	0	0
NEGATIVE|PT3/PT4|IC 2/3	13	13	12	11	9	6	5	5	5	5	5	5	5	5	4	4	4	4	4	4	4	4	4	3	3	3	2	1	0	0	0	0	0	0
POSITIVE|<PT2/PT2|IC 0/1	12	12	12	9	8	7	6	6	6	6	6	6	6	6	6	6	5	5	5	4	4	4	4	4	3	3	2	1	0	0	0	0	0	0
POSITIVE|<PT2/PT2|IC 2/3	7	7	6	6	6	6	6	5	4	4	4	4	4	4	3	3	3	3	3	3	3	3	2	2	2	2	2	1	1	1	1	1	1	0
POSITIVE|PT3/PT4|IC 0/1	25	24	22	16	14	11	8	7	7	5	2	2	2	1	1	1	1	1	1	1	1	1	1	1	1	0	0	0	0	0	0	0	0	0
POSITIVE|PT3/PT4|IC 2/3	19	19	16	14	10	10	8	8	8	7	4	4	4	4	4	3	3	3	3	3	3	2	2	1	1	1	1	1	0	0	0	0	0	0

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## [1] ""
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