

Purified protein derivative skin test prior to BCG therapy enhances the clinical efficacy of BCG therapy in patients with non-muscle invasive bladder cancer



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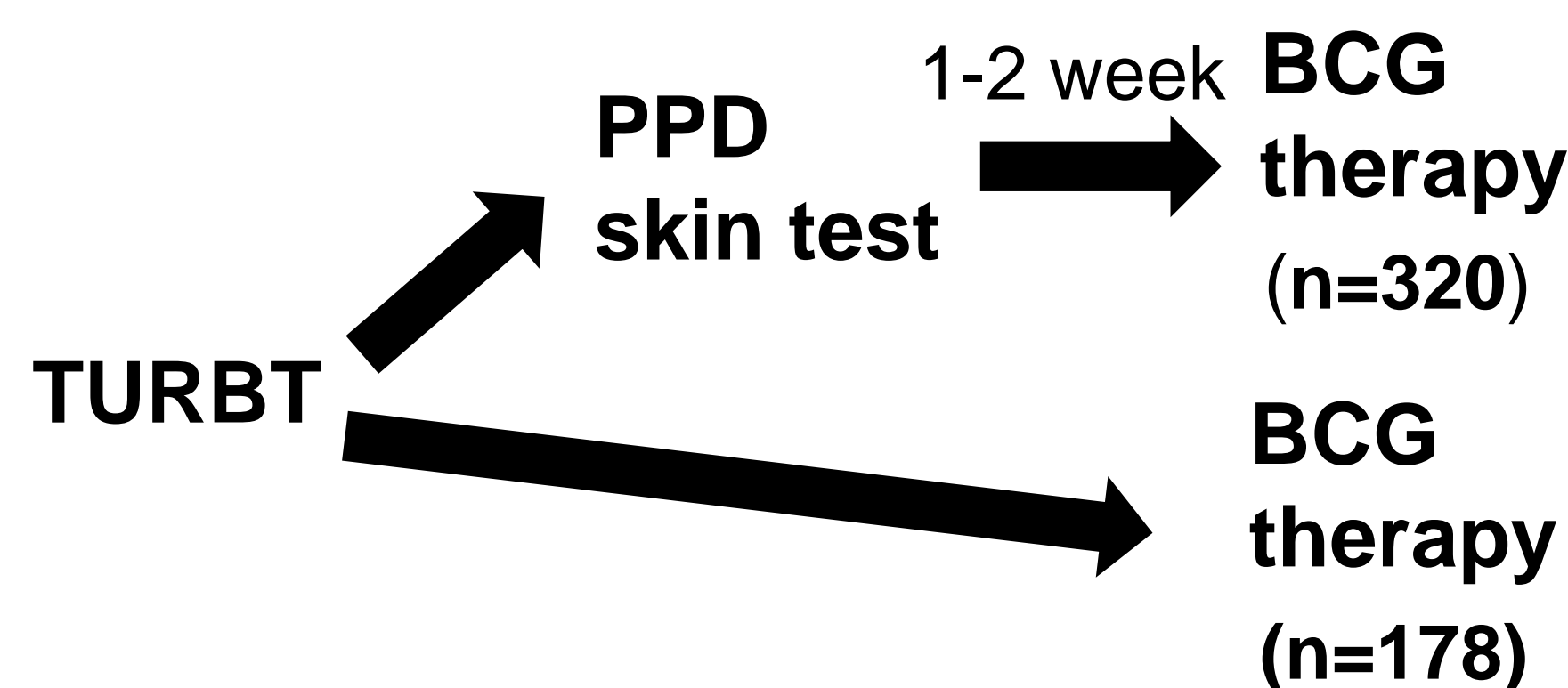
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Introduction

- The purified protein derivative (PPD) skin test is a method used to diagnose tuberculosis, and is based on delayed-type hypersensitivity.
- Repeated PPD placement can recall existing but waned immune responses and result in positive reactions in the absence of mycobacterial infection, termed the “boosting phenomenon”
- In the present study, we evaluated whether the PPD skin test prior to BCG therapy affects clinical outcomes such as oncological responses to BCG therapy and the rate of side effects associated with BCG therapy in NMIBC patients treated with adjuvant BCG therapy.

Patients and methods

- A total of 498 patients treated with adjuvant induction BCG therapy.
- 320 (64.3%) had received the PPD skin test prior to BCG therapy, while 178 (35.7%) patients had not.

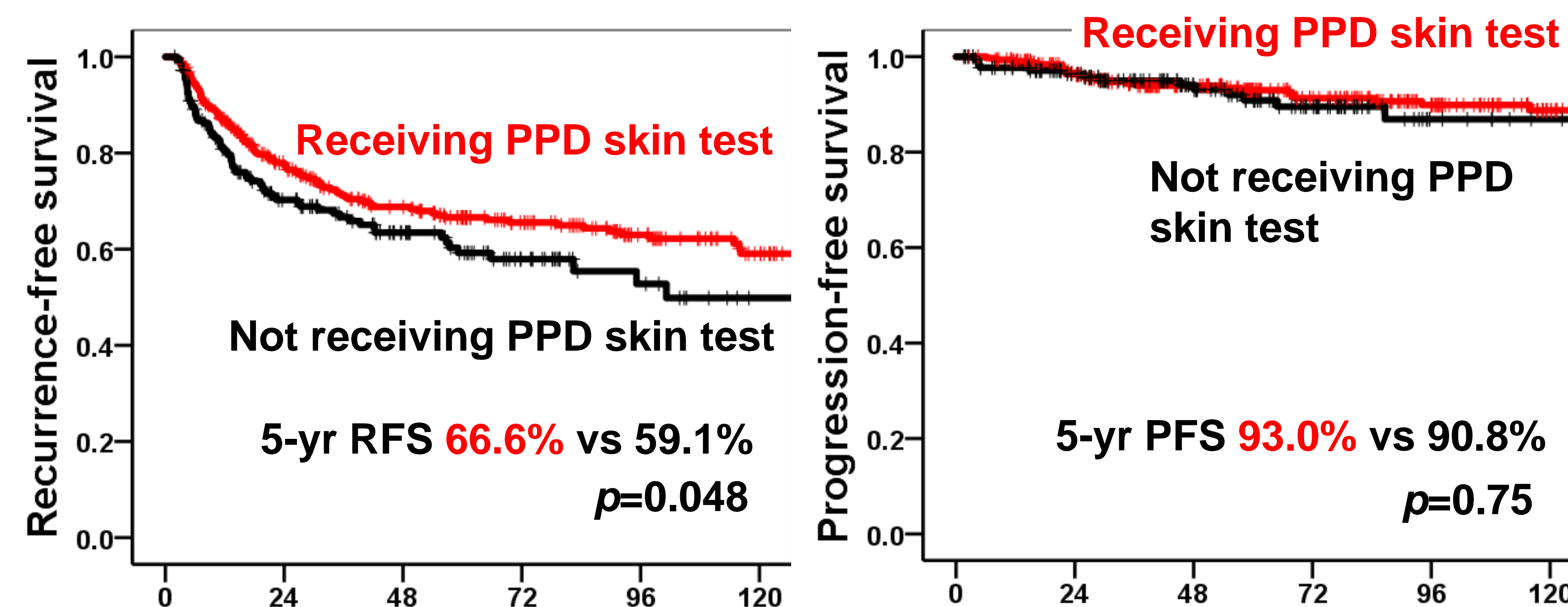


Patients characteristics

| | Receiving PPD skin test (n=320) | Not receiving PPD skin test (n=178) | p value |
|--|---------------------------------|-------------------------------------|---------|
| Age, no.(%): | | | 0.13 |
| ≤65 | 130 (41) | 60 (34) | |
| >65 | 190 (59) | 118 (66) | |
| Sex, no.(%): | | | 0.77 |
| Male | 272 (85) | 153 (86) | |
| Female | 48 (15) | 25 (14) | |
| Prior recurrence, no.(%): | | | 0.69 |
| Primary | 267 (83) | 151 (85) | |
| Recurrence | 53 (17) | 27 (15) | |
| Tumor grade, no.(%): | | | 0.85 |
| G1/2 | 132 (41) | 75 (42) | |
| G3 | 188 (59) | 103 (58) | |
| T category, no.(%): | | | <0.01 |
| pTa/is | 190 (59) | 128 (72) | |
| pT1 | 130 (41) | 50 (28) | |
| Tumor multiplicity, no.(%): | | | 0.18 |
| Single | 76 (24) | 33 (19) | |
| Multiple | 244 (76) | 145 (82) | |
| Concurrent CIS, no.(%): | | | 0.049 |
| Negative | 266 (83) | 135 (76) | |
| Positive | 54 (17) | 43 (24) | |
| BCG strain, no.(%): | | | 0.56 |
| Tokyo-172 | 202 (63) | 117 (66) | |
| Connaught | 118 (37) | 61 (34) | |
| Number of BCG instillations, no.(%) | | | 0.79 |
| 6 | 223 (70) | 122 (68) | |
| ≥7 | 97 (30) | 56 (32) | |

During the median follow-up period was 61 (IQR: 30-101) months, 178 (36%) patients developed tumor recurrence and 41 (8%) patients showed disease progression.

Oncologic outcomes



Kaplan-Meier curve showed that there is significant difference in RFS between patients who received PPD skin test and those who did not.

Multivariate analyses of disease recurrence and disease progression

| Variables | Tumor recurrence | | Disease progression | |
|---|------------------|---------|---------------------|---------|
| | HR (95% CI) | p value | HR (95% CI) | p value |
| Prior Recurrence (Primary vs Recurrence) | 1.59 (1.08-2.23) | 0.02 | | |
| Tumor grade (G1/2 vs G3) | | | 3.89 (1.63-9.30) | <0.01 |
| T category (pTa vs pT1) | | | 1.71 (0.88-3.32) | 0.12 |
| Multiplicity (Single vs Multiple) | 1.95 (1.28-2.97) | <0.01 | | |
| Concomitant CIS (Neg vs Pos) | | | | |
| BCG strain (Tokyo-172 vs Connaught) | 0.71 (0.51-0.99) | 0.04 | | |
| No. of BCG instillations (6 vs ≥7) | 0.70 (0.50-0.99) | 0.04 | | |
| PPD skin test (Not receiving vs Receiving) | 0.72 (0.53-0.99) | 0.04 | 0.48 (0.41-1.52) | 0.48 |

Multivariate analysis revealed that PPD skin test prior to BCG therapy significantly reduces the risk tumor recurrence (not progression) after BCG therapy.

BCG-related side effects

| | Receiving PPD skin test (n=320) | Not receiving PPD skin test (n=178) | p value |
|------------------------------------|---------------------------------|-------------------------------------|---------|
| Major hematuria, no.(%): | | | 0.32 |
| | 17 (5.3) | 6 (3.4) | |
| Major LUTS, no.(%): | | | 0.03 |
| | 29 (9.1) | 7 (3.9) | |
| Major fever, no.(%): | | | 0.09 |
| | 28 (8.8) | 11 (6.2) | |
| Major side effects, no.(%): | | | 0.02 |
| | 77 (24.1) | 27 (15.2) | |
| Any side effects, no.(%): | | | <0.01 |
| | 181 (56.6) | 65 (36.5) | |

Side effects during BCG therapy were classified as minor and major as follows
 Minor: Macroscopic hematuria and LUTS ≤2 days and low-grade fever ≤2 days
 Major: Macroscopic hematuria and LUTS >2 days, low-grade fever >2 days or a fever of ≥38°C, and all other side effects such as epididymitis or arthralgia were classified as major side effects.

Conclusions

- The PPD skin test prior to BCG therapy may enhance immune responses to BCG, leading to improvements in the clinical outcomes of BCG therapy in NMIBC patients