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Equally Knocking on the Door of Medical Breakthroughs: Safety and Efficacy of a New Anti-Cancer Drug Pamica ($PICNH_2Ca$) for Late Stage Cancer Patients

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Abstract

The composition of Pamica ($PICNH_2Ca_2$) is dsRNA polyI:C, non-biotics amino compounds and $CaCl_2$. It is the second generation noncytotoxic product of PICKCa (PIKA) adjuvant which was found effective in phase II clinical trial for PICKCa rabies vaccine and phase I trial for PICKCa hepatitis B vaccine in Singapore. With their knowledge and consent, cancer patients, regardless of their tumor types or performance status (ECOG above 5 or ECOG > 20), who were unresponsive to standard treatment, were treated free of charge with Pamica by injection or nasal spray. The primary results indicated that Pamica had no side effect except for a few cases of local pain in the site of injection and appeared to markedly improve cancer patients' appetite, physical strength, quality of life and extended patients' life for months and counting. These preliminary findings underlined promise of this potentially life-saving drug. In the hope of cooperating with the proper authorities, companies, and hospitals to benefit patients at the earliest opportunity, we share our findings in this paper.

Keywords

Cancer Immunotherapy, DS RNA, TLR3, Terminal Cancer, Adjuvant, PICKCa, PIKA, Pamica

1. Introduction

Despite all the progresses made in cancer detection and treatment, it remains one of the most deadly diseases. Developing effective treatment of late stage cancer has been our biggest dream since we made the discovery of the observable

adjuvant effect of PICKCa at Franch Paster Institut in 1993 [1] [2]. After over 30 years of research, we developed a noncytotoxic anti-cancer drug named Pamica ($PICNH_2Ca_2$), which is the second generation product of PICKCa. Preliminary clinical trial results suggested that Pamica is both safe and effective in treating late stage cancer with markedly improved life quality and prolonged survival. Except for a few cases of local pain near the injection site, no other side effects have been observed.

2. Experimental Section

2.1. The composition of Pamica ($PICNH_2Ca_2$)

Pamica is a double-stranded RNA drug. It consists of dsRNA polyI:C, non-antibiotic amino compounds and $CaCl_2$. These constituents are bonded together organically rather than simply mixed. The main difference between Pamica and PICKCa is that Pamica substitutes non-antibiotic amino compounds for kanamycin in PICKCa. Being non-antibioticamino compounds with more amino groups to combined with phosphate group in PolyI:C, these compounds are both safe and more effective in Pamica than kanamycin in PICKCa.

These are the differences of Ds RNA adjuvants and their finder in Table 1. It indicates that PICKCa\PIKA and Pamica specific the latter are more beneficial to patients because they are much safer and more effective than PIC, PICLC and $PIC_{12}U$.

2.2. Control of Pamica

Pamica must meet the National Standard of PICKCa injection WS1-XG-050-2000 from China Food and Drug Administration (CFDA) which is same as US FDA. The details are listed as following.

The conclusion in Table 2 was that Pamica met the Standard WS1-XG-050-2000 of CFDA.

Table 1. Difference of DS RNA adjuvants [3].

DS RNA, Finder	Components	Characteristics
PIC (Merck)	PIC	Cannot be applied to primates above
PICLC (Levy *et al.*)	PIC + lysine + carboxymethylcellulose	Effectivity, serious side effect in human bodies
$PIC_{12}U$ (Johns Hopkins University)	$PIC_{12}U$	Safety, denied by US FDA in 2012
PICKCa or PIKA (Haixiang Lin, Lietao Li)	PIC + kanamycin + $CaCl_2$	Safety and effectivity for human body, containing antibiotics
Pamica (Haixiang Lin, Fang Liu)	PIC + nonantibiotic amino compounds + $CaCl_2$	More safe and effective than PICKCa, no antibiotics

Table 2. National Standard of China FDA PICKCa injection WS1-XG-050-2000 [4].

Qualitative character
Should be colorless transparent liquid
Identify
Should be enhanced fluorescence reaction
Maximum light absorrptionin wave 266 ± 2 nm
Minimum light absorrptionin wave 228 nm
Check
pH 6.0 - 8.0
Hyperchromic effect > 55%
Transparency > 98.0%
Content should be 90% - 110% of labelled amound
Others
Abnormal toxicity test should meet rule
Molicular Weight (1 mg/ml) above 4 s tRNA
Endotoxine < 100 EU/ml
Sterility test should meet rule

3. Salvage Therapeutic Results to Late Stage Cancer with Pamica

3.1. Selection of Cancer Types

Table 3 showed that Pamica could treat many kinds of cancers including Carcinoma of salivary gland, Laryngocarcinoma, Esophaguus cancer, Liver cancer, Lung cancer, Coloretal cancer. In fact, pamica has no selection to trea cancers, Perhaps it associated with action mechanism of Pamica.

3.2. Selection of Cancer Patients

The patients received Pamica treatment were unresponsive to standard treatment. Patients were selected regardless of the type of tumor and performance status (ECOG above 5 or ECOG > 20), that is loss of self-care ability and in need of actively support treatment. All patients were informed and had given their consents to participate. The treatment was given free of charge.

3.3. Method of Application

Pamica is a non-antibiotics and non-cytotoxic dsRNA product. 2 mg/every two days, im or mist spray.

3.4. Clinical Effects

The patients were administered the drug by injection or nasal spray for 2 - 9 months. No side effects were observed other than a few cases of local pain in injection. Details are tabulated in the Table 3.

Table 3. Salvage therapeutic results to terminal cancer patients with Pamica.

Name	Sex	Age	Tumor	Before using the Pamica	After using the Pamica	Time of duration using the Pamica	Remark
Shulan Lin	Female	80	Carcinoma of salivary gland, recurrence after surgery twice. Multiple organ metastasis. The doctor thought she only had 2 months lifetime in May 2016.	Lie in bed, anorexia, nausea, emesis, eat a meal a day, spirits drooping, need to actively support treatment with blood and protein. Even to be terminally ill.	Since October 2016. eat 3 meals a day, put on weight, good mental state, lifetime has prolong 7 months so far (July 2016-February 2017) than doctor's prediction. No side effect (i.m) excepting local pain in injected part, this good state has kept to present.	From June to present (February 2017).	Beginning i.m from middle third of June. After 1 month changed to nasal spray 2 - 4 mg/ every two days.
Shufen Gao	Female	72	Laryngocarcinoma, had surgery in 2014 and relapsed in the beginning 2016.	Breath with difficulty, easy to suppress wake, can only tolerate, the physical difference.	2 mg/every two days for half of month and than the symptoms relieved, may go to market, appetite increased, difficult breathing relieved, can has a good sleeping and feel better obviously. No side effect (i.m) excepting local pain in injection site	From April 2016 to present (February 2017).	
Wenxiao Bai	Male	59	Esophaguus cancer was fond in prison and came back his village in countryside in June, 2016. Did not receive any treatment.	Tired, sweating, low appetide, only could eat one egg. Breathe with difficulty, general malaise.	After took the drug half of month, appetite notably increased, could eat 7 - 8 eggs once and drink wine, put on weight, felt better obviously, No side effect no pain in local (i.m).	From August 2016 to present (February 2017).	
Yanmin Zheng	Male	48	Liver cancer, the liver was resected one third, cholecystectomy, need to take anodyne	Physical difference, Tired, low appetite, hepatalgia symptoms.	Since taking the drug, fatigue symptom has been in remission, physical strength improved, appetite increased, pain remitted, patient can get up to take anodyne by self.	From September 2016 to present (February 2017).	
Changli Qi	Male	50	Lung cancer was diagnosed in 2016. Untreated, only take anti inflammatory and painkiller drugs.	Bed-ridden, physical difference, walk need used stick, the body weight only was 25 kg. Breath with difficulty, hydrothorax about 250 g everyday	Since taking the drug fatigue symptom is in remission, physical strength enhancement, walk without aid, appetite increased, hydrothorax has not decreased.	From August to October, 2016	
Guoting Zhao	Male	66	Coloretal cancer was made the definite diagnosis in June, 2016. And got up treatment as economic hardship	Bowel movement more than 10 times a day and with pus blood, need to take anodyne	Pus blood disappeared, cancer pain remitted, pain in site injection at beginning,	From November 2016 to present (February 2017)	

These cases (Table 3) preliminarily indicated: 1) Satisfactory safety in cancer treatments. Pamica had no side effect excepting a few cases local pain near injection site. 2) Efficacy: Pamica appeared to be able to markedly improve patients' appetite, physical strength, and state of mind, which also extended patients' life for months and counting.

4. The Basic Research of Pamica

Pamica and PICKCa are ligands of pattern recognition receptors of TLR3, MDA5 and RIG-1. PICKCa vaccines can activate innate pathways *in vivo* to produce cytokines including IFN-α, IFN-β, IFN-γ, IL-2, IL-12p40, IL-6, TNF-α, promote macrophage function, stimulate antigen-presenting cells to produce co-stimulators of CD40, CD80, CD86, activate cell-mediated immunity and humoral immunity. Due to PICKCa adjuvant enhancing productions of IFN, IL-2, IL-12, the adjuvant may make prophylactic vaccines from main humoral immunity to possess strong cell-mediated immunity as therapeutic vaccines. In three independent experiments of post-explosure immunizations of mice and beagle dogs, PICKCa rabies vaccine was much better than commercial adjuvant-free rabies vaccines, the protective rate was 70% - 100% and 20% - 30% respectively, and the statistical analysis were significantly different ($P < 0.05$ - 0.001). PICKCa rabies vaccine and PICKCa hepatitis B vaccine had succeeded in phase II clinical trial and phase I trial in Singapore. Also PICKCa and its vaccines have cooperated with US including The Scrioos Intitute to AIDS, MRIID to Ebola, AERAS to tuberculosis and US FDA has approved PICKCa hepatitis B vaccine as anti-liver cancer orphan drug [5]-[10].

Pamica is the second generation non-cytotoxic product of PICKCa. The difference between Pamica and PICKCa is that Pamica substitues non-antibiotic amino compounds for kanamycin in PICKCa. Pamica contains more amino groups which bond to the phosphate group in PIC making the double-strand more stable and not to be hydrolyzed as easily, therefore Pamica is more effective than PICKCa. In addition, without kanamycin which could cause hearing loss, Pamica is also safer than PICKCa [11].

5. Discussion

From the mechanism, it is an analog of PICKCa. Pamica ($PICNH_2Ca_2$) is effective cancer immunotherapy drug which significantly improves systemic immunity of Late Stage Cancer Patients including innate and acquired immunity also including CMI, BMI, CD8+, CD4+ and memory immunity and so on. That may be a key role to improve life quality and prolonged survival of terminal cancer patients although it is not to kill cancer cells directly.

Open question. However crude these clinical results may be, we found the findings exciting nonetheless. These tests were conducted without being monitored by hospital. They lacked the testing indexes in diagnosis and treatment. But it still showed promise that we may be at the doorstep of an effective treatment for late stage cancer.

In the future, first step should be expanding clinical trial of Pamica and be sure its safety and efficacy and then to extend it to first-line treatment or combination therapy with it to cancer patient. Although Pamica is much cheaper than mono-antibodies treated cancer, it is important for treating cancer patients.

We are publishing these crude results in the hope of cooperating with the proper authorities, companies, and hospitals to bring benefit to patients at the earliest opportunity.

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